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Bridging the gap: Leveraging the sustainability agenda to inform policies and actions on drivers of antimicrobial resistance

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Abstract

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This thesis seeks to advance our understanding of the drivers of antimicrobial resistance (AMR) and to inform development of policies that addresses these drivers, either through AMR-focused measures or through broader society wide initiatives, such as the 2030 Sustainable Development Goals (SDGs).

Paper I analyzes temporal trends across 73 countries (2000–2023), showing that stronger governance action correlates with improvements in AMR indi-cators , though stronger action was needed to reverse trend in resistance, anti-biotics use and drug resistance index compared to drivers which show overall high probabilities of improvement irrespective of action. It also introduces the concept of governance syndrome to categorize countries according to their progress in addressing AMR. **Paper II** maps and quantifies evidence on AMR drivers through an umbrella review, revealing that evidence on distal (indirect) drivers remains fragmented and comparatively weaker than for proximal (di-rect) drivers. This gap reflects methodological challenges in attributing cau-sality across long, cross-sectoral pathways due to heterogeneity across settings and data limitations.

Paper III and **Paper IV** examines AMR and SDG national action plans across 10 countries in Africa and Asia to assess how these plans prioritize actions tar-geting the drivers of AMR, identifying areas of alignment, misalignment, and their implications for policy coherence. Together the papers reveal significant challenges in the AMR policy landscape, where many drivers are addressed re-dundantly, treated in silos by either AMR or SDG policies, or overlooked alto-gether. This fragmentation is further evidenced by the fact that alignment ob-served at the objective level often weakens when translated into intended im-plementation, especially where economic and environmental goals intersect.

This thesis has several implications. It provides a foundation for developing theories and testing hypotheses on how integrated AMR policies targeting multiple proximal and distal drivers can be effectively designed and evaluated. In addition, it also provides empirical evidence for policymakers, emphasizing the need to align AMR strategies with broader sustainable development prior-ities and to strengthen cross-sectoral governance mechanisms.

Keywords: Antimicrobial resistance (AMR), Sustainable Development Goals (SDGs), antibiotics, drivers, governance, policy analysis.

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Sammanfattning

Denna avhandling syftar till att fördjupa förståelsen av drivkrafterna bakom antimikrobiell resistens (AMR) och att bidra till policyutveckling som direkt adresserar dessa genom både AMR-specifika åtgärder och anpassning till de bredare målen inom Agenda 2030 för hållbar utveckling (SDG).

Artikel I analyserar tidsmässiga trender i 73 länder (2000–2023) och visar att starkare styrning korrelerar med förbättringar i AMR-indikatorer, även om mer omfattande åtgärder krävs för att vända trender i resistens, antibiotikaanvändning och resistensindex jämfört med drivkrafter som generellt förbättras oberoende av åtgärd. Studien introducerar också begreppet governance syndrome för att kategorisera länder utifrån deras framsteg i arbetet mot AMR. **Artikel II** kartlägger och kvantifierar evidensen om AMR-drivkrafter genom en paraplyöversikt och visar att evidensen för distala (indirekta) drivkrafter är mer fragmenterad och svagare än för proximala (direkta) drivkrafter. Detta speglar metodologiska utmaningar med att fastställa kausalitet över långa, sektorsövergripande kedjor på grund av heterogenitet mellan kontexter och bristande datatillgång.

Artiklarna III och IV undersöker nationella handlingsplaner för AMR och SDG i tio afrikanska och asiatiska länder för att analysera hur politiska strategier prioriterar åtgärder mot AMR-drivkrafter och identifierar områden med samstämmighet, bristande samordning och deras konsekvenser för politisk koherens. Resultaten visar tydliga policy-luckor: många drivkrafter hanteras parallellt, isolerat inom antingen AMR- eller SDG-ramverk, eller förbises helt. Samstämmighet som observeras på målnivå försvagas dessutom vid planerad implementering, särskilt där ekonomiska och miljömässiga mål möts.

Avhandlingen har flera implikationer. Den lägger en grund för att utveckla teorier och testa hypoteser om hur integrerad AMR-politik, som riktar sig mot flera proximala och distala drivkrafter, kan utformas och utvärderas effektivt. Dessutom ger den empiriska bevis som betonar behovet av att samordna AMR-strategier med bredare hållbarhetsmål och stärka sektorsövergripande styrningsmekanismer.

Keywords: Antimicrobial resistance (AMR), Sustainable Development Goals (SDGs), antibiotics, drivers, governance, policy analysis.

Tóm tắt

Luận án này nhằm nâng cao hiểu biết về các yếu tố thúc đẩy tình trạng kháng thuốc kháng sinh (KKS) và hỗ trợ xây dựng chính sách giải quyết trực tiếp các yếu tố này thông qua các biện pháp đặc thù, đồng thời gắn kết với các mục tiêu của Chương trình Nghị sự 2030 về Phát triển Bền vững (PTBV).

Nghiên cứu I phân tích xu hướng theo thời gian tại 73 quốc gia giai đoạn 2000–2023, cho thấy mức độ hành động quản trị mạnh hơn có liên quan đến cải thiện các chỉ số KKS, mặc dù cần hành động mạnh mẽ hơn nữa để đảo ngược xu hướng gia tăng KKS và sử dụng kháng sinh so với các yếu tố thúc đẩy vốn có xác suất cải thiện cao hơn bất kể mức độ hành động. Nghiên cứu cũng giới thiệu khái niệm *mẫu hình quản trị* để phân loại các quốc gia theo mức độ ứng phó KKS. **Nghiên cứu II** tổng quan và định lượng bằng chứng về các yếu tố thúc đẩy KKS, cho thấy bằng chứng về các yếu tố gián tiếp còn rời rạc và yếu hơn so với các yếu tố trực tiếp. Khoảng trống này phản ánh thách thức phương pháp trong việc xác định quan hệ nhân quả qua các chuỗi tác động liên ngành, khác biệt bối cảnh và hạn chế dữ liệu.

Nghiên cứu III và IV phân tích các kế hoạch hành động quốc gia về KKS và PTBV tại 10 quốc gia ở châu Phi và châu Á, nhằm đánh giá cách các chính sách ưu tiên các hành động đối với các yếu tố thúc đẩy KKS, đồng thời xác định các sự nhất quán và chưa nhất quán của các chính sách. Kết quả cho thấy chính sách KKS vẫn tồn tại nhiều khoảng trống: nhiều yếu tố thúc đẩy được xử lý trùng lặp, tách biệt giữa các chính sách KKS hoặc PTBV, hoặc bị bỏ qua hoàn toàn. Sự phân mảnh này cũng thể hiện khi các mục tiêu thường suy yếu khi chuyển sang giai đoạn thực thi dự kiến, đặc biệt tại các lĩnh vực giao thoa giữa mục tiêu kinh tế và môi trường.

Luận án có nhiều gợi ý chính sách quan trọng. Đầu tiên, nó tạo nền tảng cho việc phát triển lý thuyết và kiểm định giả thuyết về cách thiết kế và đánh giá hiệu quả các chính sách AMR tích hợp. Đồng thời, kết quả mang lại bằng chứng thực nghiệm cho các nhà hoạch định chính sách về sự cần thiết của việc gắn kết chiến lược KKS với các mục tiêu PTBV và tăng cường cơ chế quản trị liên ngành.

Keywords: Antimicrobial resistance (AMR), Sustainable Development Goals (SDGs), antibiotics, drivers, governance, policy analysis.

“Man’s dearest possession is life. It is given to him but once, and he must live it so as to feel no torturing regrets for wasted years, never know the burning shame of a mean and petty past”;
Pavel Korchagin – cited by Nguyen Phu Trong (1944-2024)

*“Cái quý nhất của con người là cuộc sống và danh dự sống, bởi vì đời người chỉ sống có một lần. Phải sống sao cho khỏi xót xa ân hận vì những năm tháng đã sống hoài, sống phí, để khỏi hổ thẹn vì những việc làm ti tiện, đớn hèn, bị mọi người khinh bỉ” – **TBT. Nguyễn Phú Trọng***

List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

I. Søgaard Jørgensen, P., **Thanh, L.N.**, Pehlivanoğlu, E., Klein, F., Wernli, D., Jasovsky, D., Aktipis, A., Dunn, R.R., Gröhn, Y., Lhermie, G., Scott, H.M. and Klein, E. Y. (2025). Association between national action and trends in antibiotic resistance: an analysis of 73 countries from 2000 to 2023. *PLOS Global Public Health*, 5(4), p.e0004127.

II. **Nguyen-Thanh, L.,** Wernli, D., Målqvist, M., Graells, T. and Jørgensen, P.S (2024). Characterising proximal and distal drivers of antimicrobial resistance: An umbrella review. *Journal of Global Antimicrobial Resistance*, 36, pp.50-58.

III. **Thanh, L.N.**, Wernli, D., Målqvist, M. and Jørgensen, P.S. (2025). 'When global health meets global goals': assessing the alignment between antimicrobial resistance and sustainable development policies in 10 African and Asian countries. *BMJ Global Health*, 10(3).

IV. **Thanh, L.N**., Wernli, D., Målqvist, M. and Jørgensen, P.S. A Large Language Model approach to quantify interactions between AMR and SDG action: Knowledge for seeking synergy solutions. Manuscript in preparation to *npj Antimicrobials and Resistance*.

Contents

Abbreviations

ABR	Antibiotic Resistance
AMR	Antimicrobial Resistance
AMU	Antimicrobials Use
EU/EEA	European Union/European Economic Area
FAO	Food and Agriculture Organization
GAP	Global Action Plan
HICs	High-income countries
LICs	Low-income countries
LMICs	Low and middle-income countries
MICs	Middle-income countries
NAP	National Action Plan
OECD	Organization for Economic Co-operation and Development
SDGs	Sustainable Development Goals
UAC	Uppsala Antibiotic Center
UN	United Nations
WASH	Water, Sanitation, and Hygiene
WB	World Bank
WHO	World Health Organization
OIE	World Organization for Animal Health

Introduction

The waning miracle of modern medicine

The discovery of penicillin by Alexander Fleming in 1928 marks one of the most significant scientific achievements of the 20th century, a breakthrough that revolutionized medicine and saved millions of lives from fatal infectious diseases. Prior to the introduction of antibiotics, approximately 1 in 20 infants died before their first year of life, a rate that has since declined to 3.5 per 1,000 live births nowadays (1). The early success of antibiotic discovery, coupled with significant commercial incentives, encouraged indiscriminate and often careless use of these drugs. This misuse created intense selective pressure that fueled the emergence of antibiotic resistance, a natural process in which bacteria develop mechanisms to resist the antibiotics, resulting in more difficult-to-treat infections (2,3). The ensuing evolutionary "arms race" between humans and microbes, whereby new drugs are developed, and microbes subsequently evolve to resist them, seems never reach an endpoint. However, after the so-called golden era of antibiotic discovery between the 1940s and 1960s, the world entered a "discovery void", with very few new antibiotics were introduced since the 1980s and a steady decline in pharmaceutical investment in research and development (4,5).

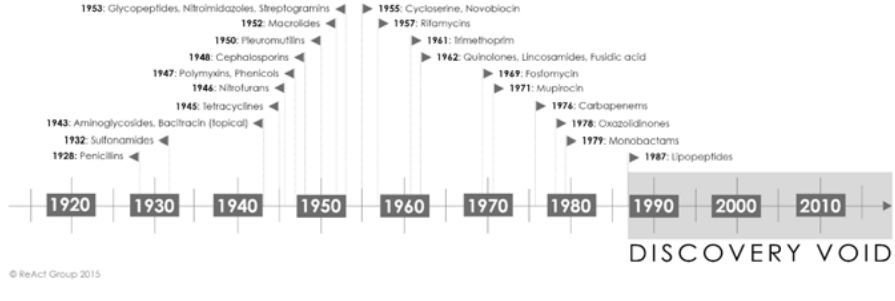

Figure 1. Timeline of new antibiotic research and development. *The discovery void has started since 1987 until today. Source: ReAct website* (6)

As a consequence, the clinical efficacy of antibiotics has gradually been undermined, threatening to reverse decades of medical progress. This situation is increasingly alarming, as many pathogens have acquired resistance to

multiple classes of antibiotics. Based on their degree of resistance, pathogens can be classified into four "zones" according to their proximity to the threshold of untreatability (**Table 1**) (7,8). At the most severe level is the *surpassed zone*, which includes 7 of the 20 pathogens assessed. This group consists of six Gram-negative bacteria and one type of fungus, for which *treatment choices are extremely limited*. The next category is the *uncertain zone*, which encompasses pathogens that *remain treatable but are increasingly difficult to manage*. This group is further divided into high, medium, and low levels of risk. Pathogens in the high-risk group are close to untreatable, while those in the medium-risk category, which include multidrug-resistant (MDR) and extensively drug-resistant (XDR) organisms, demonstrate the urgent need for novel antimicrobial agents. The low-risk group includes two Gram-positive bacteria that have only recently started to show resistance to important antibiotics. Finally, the *safe zone* covers microorganisms that *remain fully susceptible to existing treatments*, display only minor resistance to non-critical drugs, or have not yet developed clinically significant resistance. This last group represents the majority of microorganisms not included in current global prioritization lists.

Over the decades, the issue has broadened beyond bacteria to include resistance in viruses, fungi, and parasites, forming the wider concept of antimicrobial resistance (AMR). Despite this conceptual distinction, the term *"antimicrobial resistance*" is predominantly used, and often interchangeably with *antibiotic resistance* in both scientific literature and policy context.

Antimicrobial Resistance: A global One Health issue

The growing threat of AMR has been aptly described as a "silent pandemic" and a global public health concern (9). Unlike other pandemics that erupt suddenly and attract immediate global attention, AMR is a slow-moving, cumulative trajectory. Before the COVID-19 pandemic in 2019, data indicated AMR as the third leading cause of death worldwide annually, responsible for an estimated 4.95 million deaths overall, with 1.27 million deaths directly attributed to antibiotic-resistant bacterial infections (10). The highest burden was recorded in Western Sub-Saharan Africa at an estimated 27.3 deaths per 100,000 (10). In OECD (Organization for Economic Co-operation and Development) and EU/EEA (European Union/ European Economic Area) countries, resistant infections claim approximately 79,000 lives annually, a figure that is 2.4 times the combined mortality from tuberculosis, influenza, and HIV/AIDS in the same region in 2020 (11). This number is projected to rise substantially over the next 25 years, with about 39.1 million deaths from antibiotic-resistant infection globally (12). The health burden of AMR can be exacerbated during periods of crisis such as natural disasters, armed conflicts, or pandemics. Evidence from the COVID-19 period shows how strained systems and disrupted services can amplify inappropriate antibiotic use and healthcare-associated

transmission, reinforcing the need to protect core infection prevention and control, vaccination, and water and sanitation services during emergencies (13–15).

Beyond health, AMR has multiple socioeconomic consequences. The issue of AMR is not limited to the healthcare setting (16–19); it is widespread across humans, animals, plants, food, and the environment (20–24) and does not respect geographic borders (25–28). Rising levels of AMR could also impede the progress towards many of the Sustainable Development Goals (SDGs), particularly those focusing on health and well-being, poverty reduction, food security, environment and economic growth (9,29,30). A report by World Bank indicated that by 2050, without effective containment, global economy could decrease by US$ 1.7 trillion annually - an equivalence to a 0.88% reduction in Gross domestic product (GDP) (31), and a widening of global inequality, especially in low-income countries (26,29,31). Sectors such as tourism, domestic hospitality, and livestock production may also be significantly impacted, with global livestock output potentially declining by up to 11% (31,32) (**Table 1**).

The development, transmission and impact of AMR are determined by a variety of drivers in the ecosystem, including those related to people and society, animal and environmental health, governance and health systems (33–35). The use, misuse, or overuse of antimicrobial drugs across sectors, including human healthcare and livestock production is considered to be a major driving force of AMR (36–39). Human antibiotic consumption has risen markedly in the past two decades. The global rate increased by roughly 46% between 2000 and 2018, with the sharpest growth in low- and middle-income countries (40). Over-the-counter sales of antibiotics without a prescription remain common in many settings, and substandard or falsified medical products are reported across regions, which undermines treatment and can promote resistance (41). Antimicrobials are also widely used in food-producing animals for treatment, metaphylaxis and, in some settings, prophylaxis. Early global projections suggested that antimicrobial consumption in livestock could increase by about 67 percent between 2010 and 2030 as demand for animal-source foods rises and production intensifies, particularly in low- and middle-income countries (LMICs) (42). The environment also plays a critical role in the AMR issue, acting as both a reservoir and transmission pathway for resistant organisms and genes. Antibiotic residues and resistant bacteria can enter waterways and soils through human sewage, hospital and community wastewater, effluent and sludge from pharmaceutical manufacturing, manure and runoff from farms, and discharges from aquaculture (43,44). Hence, AMR is increasingly recognized as a One Health challenge that requires coordinated, multisectoral responses.

Table 1. The current threat of AMR and its impacts. HR= high risk, LR= low risk MR= medium risk, MDR= Multidrug resistance; PDR=pan-drug resistance; XDR=extensively-drug resistance.

*= except *Escherichia coli, Klebsiella pneumoniae*, and genus *Salmonella* and *Shigella*.
***The number was estimated using published country-level DRI reported by Klein et al.* (45). *Each country's data is weighted by the inverse of its variance. Due to the provided data doesn't include the exact sample sizes or standard errors, weighting was approximated by using the range of the confidence intervals as a proxy for variance. A smaller range in the confidence interval indicates more certainty in the DRI value, and thus, that value should have a higher weight in the aggregated calculation.*

AMR pressure	**Control variable**	**Criteria for assessment**	**Current trend** Highest resistance reported
Treatability of critical pathogens			
Gram Negative bacteria	*Acinetobacter* spp.	Surpassed	PDR (46–48)
	Pseudomonas aeruginosa	Surpassed	PDR (49,50)
	Klebsiella pneumoniae	Surpassed	PDR (51)
	Escherichia coli	Surpassed	PDR (52)
	*Enterobacteriaceae**	Surpassed	PDR (53,54)
	Neisseria gonorrhoeae	Surpassed	XDR (55,56)
	Salmonella spp.	Uncertain: HR	XDR (57)
	Shigella spp.	Uncertain: MR	MDR (58)
	Campylobacter spp.	Uncertain: MR	MDR (57,59)
	Helicobacter pylori	Uncertain: MR	MDR (60)
	Haemophilus influenzae	Uncertain: MR	XDR (61)

Gram Positive bacteria	*Clostridioides difficile*	Uncertain: HR	MDR(62)
	Enterococcus spp.	Uncertain: HR	XDR (63)
	Staphylococcus aureus	Uncertain: HR	XDR (64)
	Streptococcus pneumoniae	Uncertain: MR	MDR (65)
	Streptococcus Group A	Uncertain: LR	MDR (66)
	Streptococcus Group B	Uncertain: LR	MDR (67)
Other	*Mycobacterium tuberculosis*	Uncertain: HR	XDR (68)
Fungi	*Candida spp.*	Uncertain: MR	MDR (69)
	Candida auris	Surpassed	PDR (70,71)
Antibiotic effectiveness	Drug resistance index (DRI)	From 0 (complete susceptibility) to 100 (absolute resistance)	40.53** (45,72,73)
Burden of AMR	Health impact	excess mortality and morbidity related to AMR infection (74)	4.95 million deaths associated with bacterial AMR, including 1.27 million deaths attributable to bacterial AMR in 2019 (10) (75).
	Economic impact	loss of GDP and additional health-care costs related to AMR infection (74)	global economic could decrease by US$ 1.7 trillion annually, an equivalence of 0.88% GDP reduction (31); healthcare expenditures could increase from US$ 66 billion to US$ 159 billion (32); global livestock output potentially declining by up to 11% (31,32)

The global response to AMR: progress and gaps

For decades, AMR was largely framed as an innovation challenge confined to microbiology and clinical medicine (76). This narrow focus limited international coordination and obscured the broader social, economic, and environmental dimensions of resistance (77,78). The adoption of the Global Action Plan (GAP) on AMR by the WHO in 2015 marked a paradigm shift, reframing AMR as a One Health issue requiring integrated, multisectoral governance. The GAP established both a normative framework and a political mandate for all Member States to develop National Action Plans (NAPs), structured around five core pillars: awareness, surveillance and research, infection prevention, antimicrobial stewardship, and sustainable investment (79):

1. *Objective 1: "Improve awareness and understanding of antimicrobial resistance through effective communication, education, and training".* This emphasizes the need to raise AMR awareness among healthcare workers, veterinarians, policymakers, and the public, ensuring that knowledge gaps are addressed and behaviors contributing to resistance are reduced.
2. *Objective 2: "Strengthen the knowledge and evidence base through surveillance and research*". This involves establishing robust national surveillance systems for both AMR and AMU and fostering research to understand the drivers of resistance and develop new interventions.
3. *Objective 3: "Reduce the incidence of infection through effective sanitation, hygiene, and infection prevention measures".* This objective underscores the importance of preventing infections before they occur, thereby reducing the need for antibiotics. It highlights interventions such as improving water, sanitation, and hygiene (WASH) systems, strengthening infection prevention and control (IPC) in healthcare settings, and promoting vaccination programs.
4. *Objective 4: "Optimize the use of antimicrobial medicines in human and animal health"*. This objective focuses on antimicrobial stewardship to ensure that these medicines are used responsibly and only when necessary, preserving their effectiveness for as long as possible.
5. *Objective 5: "Develop the economic case for sustainable investment that takes into account of the needs of all countries and increases investment in new medicines, diagnostic tools, vaccines, and other interventions*". This acknowledges the "market failure" in antimicrobial research and development and calls for innovative models to stimulate development.

This initiative, jointly advanced by lead international organizations including World Health Organization - WHO, World Organization for Animal Health - OIE, Food and Agriculture Organization of the United Nations - FAO has

catalyzed global engagement. As of 2023, 178 countries had developed AMR-NAPs, reflecting a remarkable global political commitment. However, implementation remains limited, with only 27% of NAPs operational and 11% supported by dedicated budgets due to systemic governance deficits (80), particularly in accountability mechanisms and cross-sectoral resource allocation, which continue to hinder the translation of policy adoption into effective implementation. Key actions to address AMR in the GAP and associated NAPs remain focused on interventions with direct links to AMR, including AMU and stewardship to reduce this. These interventions involve the utilization of policy levers such as legislation, taxation, economic incentives, funding support, public awareness campaigns, and the regulation of professionals and businesses whose practices could affect AMR (81). While desirable, from a public health perspective, efforts to reduce AMU are insufficient to curb the rise of AMR, as AMU can explain only some of the variation in resistance levels across countries and regions (82). Moreover, a complete cessation of AMU is neither feasible nor desirable, as antimicrobials are crucial in treating and controlling infectious diseases in humans, animals, and plants (83,84).

The challenge of AMR is, on the other hand, shaped by other contextual factors (34,35). Different countries are at different stages in the progression of AMR, facing different challenges and adopting diverse response strategies. High-income countries (HICs) have historically been involved in tackling AMR for a long time; for example, the United Kingdom's Swann Committee Report (1969) played a pioneering role in recognizing and regulating antibiotic use in livestock (85). More recently, in Switzerland, a recent national referendum proposed phasing out pesticide use and ending subsidies for farms relying on prophylactic antibiotics (86). Although the bill was ultimately rejected, the proposal and ensuing debate, with strong variation between cities and the countryside, serve to highlight where the country is in its fight against AMR. In contrast, low-income countries (LICs) face more fundamental barriers. Limited access to clean water and sanitation, persistent infectious disease burdens, particularly among children under five, and inadequate diagnostic capacity in both human and animal health systems constrain surveillance and effective response (33,87,88). Meanwhile, middle-income countries (MICs), such as China and Brazil, encounter a different set of challenges: agricultural production is a cornerstone of their economies and international trade, yet remains heavily dependent on antimicrobial use (89). These examples highlight the heterogeneity of national contexts in access to basic human (and animal) needs, reliance on AMU for economic advancement, and political feasibility of different interventions. The multitude of drivers creates a very complex health challenge with multiple inter-dependencies throughout the system (90–94). As a result, interventions will likely have unexpected consequences across the system, and no intervention can be reliably transferred to a new setting, without adapting to the unique context (95).

Sustainability agenda and the link with AMR

Preserving antimicrobial efficacy while sustaining many benefits that humans derive from microbes represents a critical sustainability challenge (96). Addressing the global challenge of AMR, therefore, requires dealing with coevolution, specifically how the fundamental feedback loops between microorganisms and human behaviors and actions take place in strongly coupled social–ecological systems (96,97). The dominant paradigm in AMR governance has long been shaped by the question: "How do we stop bacteria from becoming resistant?". While this framing has led to important measures including antimicrobial stewardship or the development of new drugs, they are limited in their capacity to address the systemic and cross-sectoral driving forces of the resistance. A social-ecological perspective which views human societies and ecological systems as interdependent and co-evolving, instead broadens the scope of the issue, positioning AMR as both an exceedance of ecological limits and a shortfall in social foundations (8,98). The question can therefore be reframed: How can societies pursue health, poverty reduction, food security, and economic growth within a "*safe and just operating space"*, recognizing that AMR poses a major threat to sustaining human health over the long term?

This broader framing aligns closely with the sustainability agenda. The 2030 Agenda, adopted by the United Nation, provides a pivotal framework for pursuing sustainable development while ensuring that AMR does not surpass ecological boundaries (29,99). It is a major agenda for actions on societal challenges that has the potential to be an important instrument for reducing the development of AMR by targeting many of its drivers in human, animal and environmental health (30,98,100). Each year, about US$4 trillion are invested to achieve the SDGs, with an ongoing commitment to increase as global efforts are ramped up (101). Given the broad scope of the SDGs, these SDG investments far outpace the dedicated finance for implementing AMR-NAPs, only about US$ 47 billion annually according to a report published by the Global Leaders Group on Antimicrobial Resistance (102). With the 2030 Agenda poised to remain a pivotal global policy framework for guiding development over the next decade (103), the SDG and AMR agendas represent two major, interconnected frameworks that are likely to influence the development and transmission of AMR.

Therefore, there is an opportunity to use the SDG agenda to urgently improve the governance and pace of the response to AMR (104). By setting the overall direction for societal development, commitment to meeting the SDGs could have an impact on AMR comparable to that of the actions within the GAP-AMR (105). The relationship between AMR and sustainable development is bidirectional (**Figure 2**). Inputs and activities to achieve SDG goals that directly link to human health (e.g. clean water and sanitation, good health and wellbeing, zero hunger and no poverty) as well as those that recognize the interconnections between human, and animal and ecosystem (e.g. climate

action, life below water and life on land) will have impacts on a multitude of AMR drivers across different social-ecological contexts.

Unlike AMR-specific interventions, which are often sectoral and narrowly biomedical, the SDGs are universal, politically endorsed at the highest levels, and explicitly cross-sectoral. Their integrated and indivisible nature emphasizes that progress in one domain is inseparable from progress in others (106). By design, some of the root causes of AMR can be addressed by actions taken to meet health and equity targets set as part of the SDG agenda, thus providing a framework for multisectoral responses that can reduce resistance drivers while generating broader social and ecological co-benefits (30,97). For instance, progress toward SDG 3 (Good Health and Well-Being) including the expansion of universal health coverage, is integral for increasing access to healthcare, thereby facilitating the responsible use of antimicrobials and reducing the emergence of resistance; while at the same time addressing AMR is fundamental to lowering infection-related mortality and ensuring the attainment of SDG 3 targets (107).

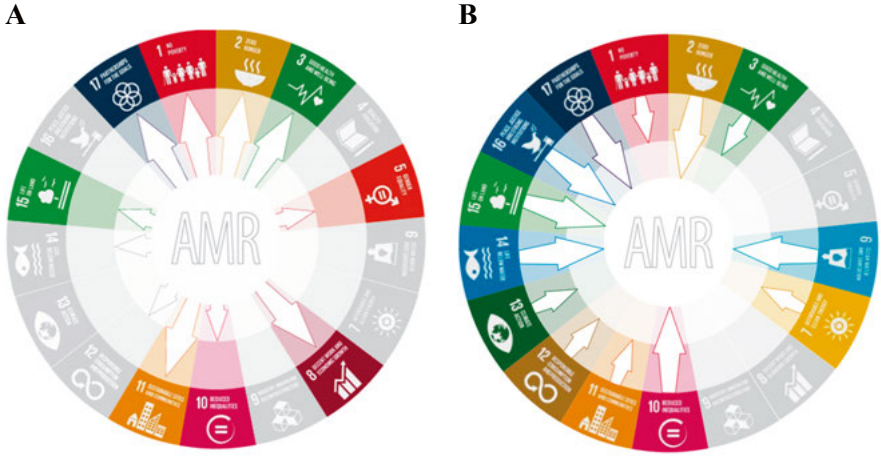

Figure 2. The bidirectional relationship between AMR and SDG. *Figure 3A: The emergence and spread of AMR will impede progress toward the 2030 agenda. Figure 3B: Progress made on some SDGs will contribute to containing AMR. Source: World Bank Report* (82)

Moreover, the complexities of managing international trade of animals and medical products, alongside the intricacies of medicine over-consumption and access, emphasize the significance of trade-related factors in shaping AMR solutions, such as through trade agreements and intellectual property rights. For example, these dimensions are governed under World Trade Organization (WTO) frameworks, most notably the Sanitary and Phytosanitary (SPS) Agreement and the Agreement on Trade-Related Aspects of Intellectual

Property Rights (TRIPS) (108). In addition, SDG 6 (Clean Water and Sanitation) emphasizes universal access to safe water and sanitation, a fundamental preventive measure that can significantly reduce antibiotic use by lowering infection rates (109).

Challenges to formulate and implement integrated interventions on AMR

Despite progress in elevating AMR on the global policy agenda, translating high-level commitments into coherent, integrated national action remains a major challenge. Many countries struggle to formulate and implement policies that cut across the human, animal, and environmental sectors due to fragmented governance structures, sector-specific mandates, and limited coordination between ministries (110–112). Weak political accountability, insufficient financing, and the absence of long-term institutional mechanisms further constrain implementation, particularly in low- and middle-income countries.

Technical and operational barriers compound these governance challenges. Differences in surveillance capacity, data quality, and regulatory standards across sectors hinder the development of shared indicators and evidence-based decision-making. As a result, many AMR interventions remain sectoral, project-based, and poorly aligned with broader health, agricultural, and environmental strategies. Building truly integrated responses requires overcoming institutional silos, establishing cross-sector accountability, and embedding AMR governance within a broader agenda for health system strengthening and sustainable development (96,113). Anchoring AMR responses in the SDG agenda offers one potential pathway toward this goal.

However, this potential is far from being realized. This challenge can be attributed to several factors. First, there is an absence of global guidance on how the integration can be done. Due to the fact that SDG-NAPs are often tailored to national contexts, with less developed countries often prioritizing a narrower set of SDGs focused on economy or governance, which may result in a lower commitment to AMR objectives (114). For instance, agricultural intensification policies to achieve food security could lead to greater antimicrobial use unless carefully regulated (115), while investments in health care access could increase antibiotic consumption in the absence of strong stewardship mechanisms (116).

Second, competing priorities and institutional fragmentation may delay the engagement of SDGs relevant sectors in responding to the AMR challenge (117–120). Currently, AMR remains largely invisible in the SDG framework. This omission risks can create blind spots where well-intentioned SDG actions may inadvertently conflict with AMR control (6). Yet few studies have systematically examined where synergies between AMR and SDG priorities

exist, where trade-offs may occur, or how policy coherence between the two agendas can be institutionalized. Understanding the impact of interventions designed to contribute to sustainable development on AMR is a critical step that will help to integrate the two agendas. Doing so will require the development of methods to link upstream interventions to downstream AMR outcomes, which should be a major goal of the AMR research community. Without such efforts, AMR risks remaining siloed from the broader SDG agenda, while sustainable development initiatives proceed without addressing one of the most significant threats to their achievement (97).

Aim and objectives

Overall aim

This thesis seeks to advance understanding of the drivers underlying the emergence and global spread of AMR and to inform policy development that addresses these drivers directly through AMR-specific measures and alignment with the broader objectives of the 2030 Sustainable Development Goals.

Specific objectives

i) Investigate the association between the implementation of AMR-specific national actions and temporal trends in key indicators including in drivers, pressures and state of AMR;

ii) Quantify the existing body of evidence linking drivers to AMR and build a network of their interconnections between direct (proximal) and indirect (distal) drivers;

iii) Compare priorities in AMR and sustainable development policy documents and their implications for drivers of AMR;

iv) Quantify the degree of synergy and conflict between AMR and sustainable development-related policy priorities targeting AMR drivers.

Methodology

To achieve the above objectives, four corresponding studies were conducted respectively to find the answers. Study I employs a quantitative ecological approach to analyze the association between national actions and temporal trends in key AMR indicators, including drivers, pressures and the state of the problem across 73 countries. Study II maps and quantifies evidence regarding different drivers of AMR through an umbrella review. Studies III and IV apply a case study design to examine how AMR and SDG policies are formulated, prioritized and interact in targeting AMR drivers in 10 countries across Africa and Asia. The overall design of 4 studies is described in **Figure 3**.

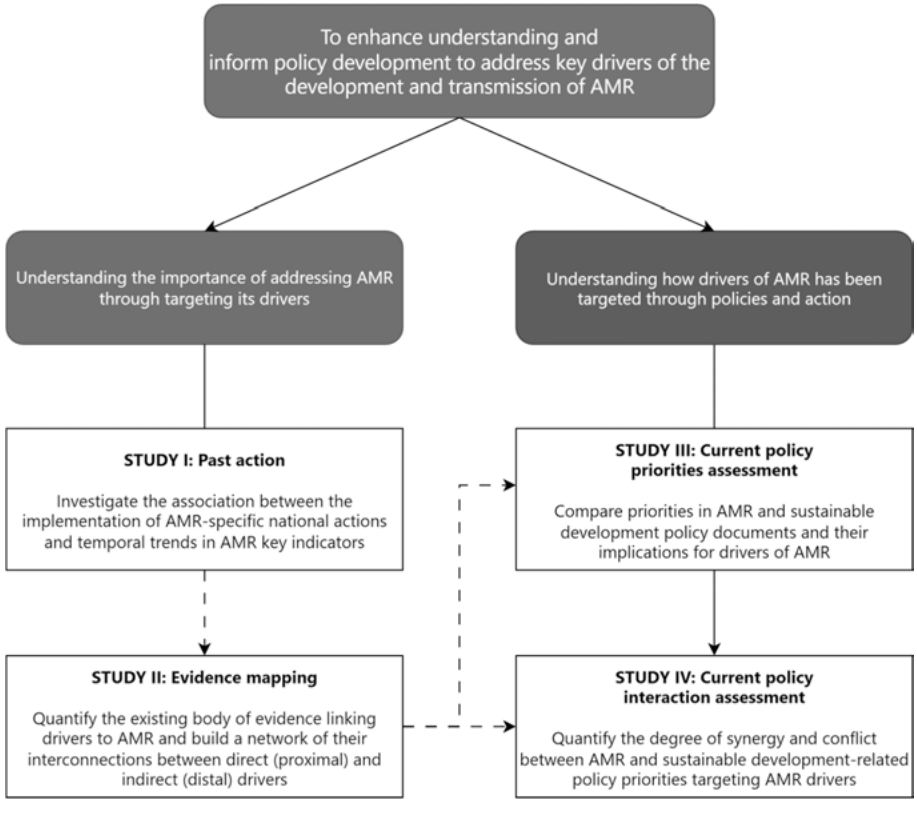

Figure 3. Overview of the studies included in the thesis

Paper I: What is the association of national action and trends of AMR indicators?

Study design

The analysis was conducted across 73 countries that had responded to the WHO TrACSS surveys from 2016–2023 and met minimum data availability criteria. Countries were selected if they reported sufficient health system indicators and at least one measure of antibiotic use or resistance covering both an early (2000–2008) and a later (2008–2016) period. The final sample covered all continents, with roughly equal representation of high-income (n=37) and low- and middle-income countries (n=36). Although the focus was on the human health sector due to limited monitoring in animals, additional analyses were conducted to explore how animal protein production related to policy action levels.

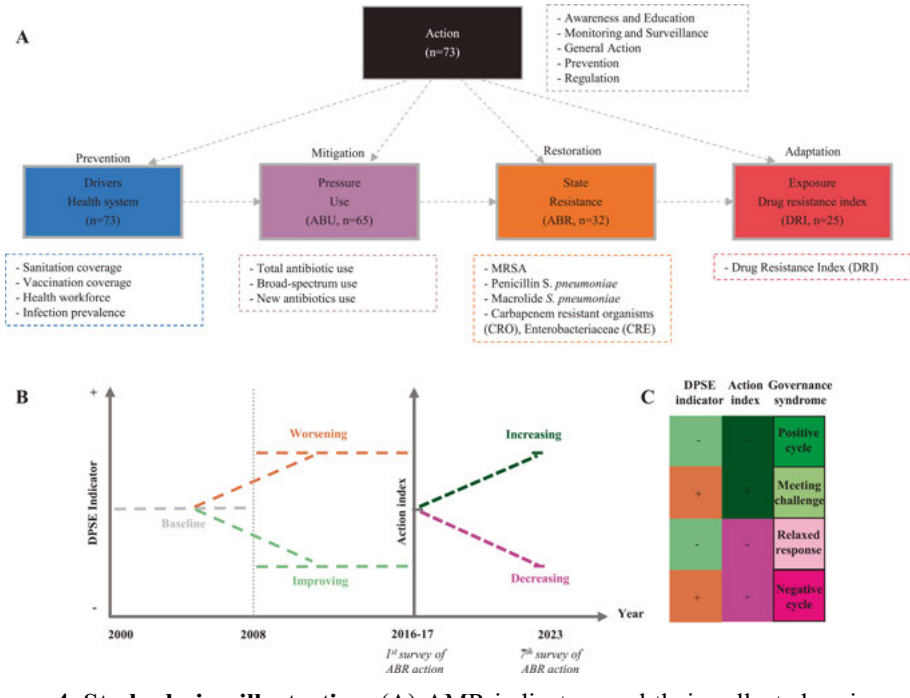

Figure 4. Study design illustration. (A) AMR indicators and their collected variables (boxes with dashed-lines). (B) Temporal overview of analysis showing the two periods across which the trend in AMR indicators is calculated and the timing of the first (2016-17) and seventh (2023) TrACSS survey. (C) Governance syndrome: Categorical trends in AMR indicators and the action index combine to form four types of governance syndrome. *Figure reproduced from the published manuscript.*

Data source, variables and indicators

Indicators were organized following a modified DPSEEA framework (Drivers–Pressures–State–Exposure–Action).

- **Drivers** captured health system conditions such as infection prevalence, sanitation, vaccination coverage, and health workforce, using data from the UN, WHO, and World Bank.
- **Pressures** measured human antibiotic consumption (2000–2015), obtained from the IQVIA database. Indicators included broad-spectrum use, use of recently introduced antibiotics, and overall per capita consumption.
- **State** reflected levels of resistance, using ResistanceMap data on MRSA, carbapenem-resistant Enterobacteriaceae and other bacteria, and streptococcal resistance.
- **Exposure** was represented by the Drug Resistance Index (DRI), combining data on resistance and consumption across 16 drug–bacteria pairs.
- **Action** was derived from the TrACSS survey, summarizing national self-reported activities across five domains: awareness, monitoring, prevention, regulation, and general governance. An overall action index was calculated by averaging across these categories. Additional explanatory covariates were sourced from international datasets, including GDP, income inequality, climate, livestock production, and population density.

Statistical analysis

For each indicator, average values were calculated for the baseline (2000–2008) and follow-up (2008–2016) periods. Differences between periods defined *linear trends* (continuous changes, standardized by standard deviation) and *categorical trends* (direction of change only). Associations between policy action and indicator trends were examined using mixed-effects regression models. Gaussian models were used for linear trends, while binomial models assessed the probability of indicator decline. Models accounted for baseline levels and included country income group as a random effect. Sensitivity analyses compared the explanatory power of policy action with alternative covariates such as health system strength, economic indicators, animal production, climate, and population factors. Model selection was conducted using the Akaike Information Criterion corrected for small sample sizes (AICc), followed by weighted averaging across the best-supported models.

In addition, the study assess the extent to which changes in AMR indicators are associated with subsequent changes in level of action from 2016 up until

2023 (**Figure 4**). A *positive cycle* was defined as countries showing declining AMR indicators from 2000–2016 followed by stronger action in 2016–2022. Conversely, a *negative cycle* referred to rising AMR indicators paired with reduced action. When both indicators and actions increased, this was classified as *meeting challenge*, while simultaneous declines in both were considered *relaxed responses*. All code and data necessary to carry out the analyses are publicly available at https://github.com/PSJorgensen/national-actions-and-trends-in-antibiotic-resistance while results can be viewed interactively at https://gedb.shinyapps.io/amr_trend.

Paper II: Which drivers of AMR are discussed in the current literature?

Study design

We conducted a systematic review of the literature to map how drivers of AMR are discussed in current literature. Six bibliographic databases were searched, covering both multidisciplinary sources (EMBASE, Web of Science, Scopus) and domain-specific collections in health, agriculture, and environment (MEDLINE, Cochrane, CINAHL). Additional studies were retrieved through snowballing techniques, including web searches, contacting authors, and checking reference lists during the full-text screening (**Figure 5**). Unlike a traditional systematic review, we adapted an "umbrella review" protocol (121) to capture all review-type publications that report the interactions of drivers in the form of correlations, causal relationships or the positive/negative feedback cycles within a sequence of events.

Analytical framework

To examine the relationships between AMR drivers, we combined two frameworks. The Driver–Pressure–State–Impact–Response (DPSIR) framework was used to map causal chains, linking underlying drivers, antimicrobial use as pressure, and AMR as the resulting state (77,93,122,123). In addition, we applied the AMR-Intervene framework to identify the main sectors and governance challenges (the policies required to tackle these drivers) linked to each driver (124). The six governance challenges include: surveillance (AMR-related monitoring activities); infection prevention (including vaccination, sanitation, hygiene, and infection control in healthcare settings); conservation (curbing misuse and overuse of antimicrobials and reducing antibiotic pollution); containment (restricting the spread of resistance); access (improving health services and equitable access to medicines); and innovation (policies and interventions supporting the development of technologies directly aimed at tackling AMR)

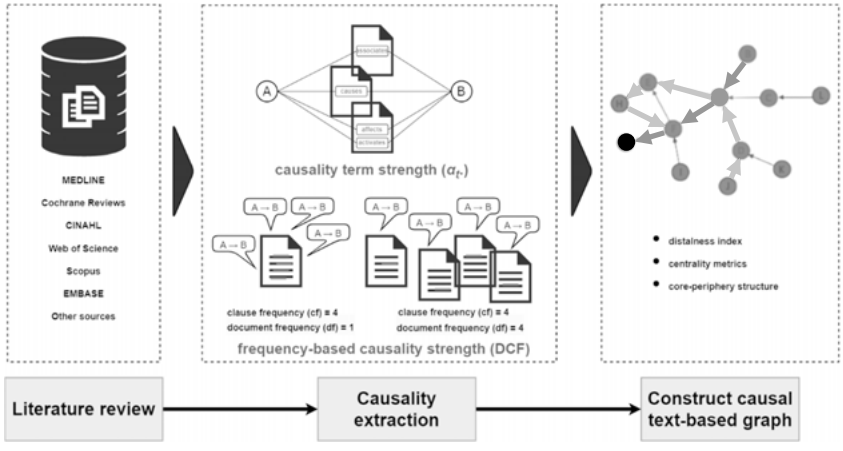

Figure 5. Database and study selection flow diagram.

Data analysis

To uncover hidden causal relationships in AMR processes, we conducted a qualitative content analysis of review articles, extracting pairwise interactions (e.g., driver–driver, driver–pressure, driver–state, and pressure–state). Using MAXQDA for coding and Excel for data organization, we extracted sentences or paragraphs that either implicitly or explicitly mentioned causality relationships. These relationships were then analyzed and visualized in R (v4.2.1) using the *tidygraph* package (v1.2.3) (125,126). We consolidated AMR outcomes into a single endpoint node, excluded incomplete chains, and applied K-means clustering to group similar links. To measure the distalness of each node, we introduced the node distalness index (D_i). This index is defined as the average path length from a given driver node to the ending node in the network (the AMR outcome) as shown in equation (1) below. This index serves as a proxy for causal influence, where a lower D_i value indicates a more direct or immediate causal connection. Finally, network centrality metrics, including eigenvector and betweenness centrality, were used to identify the most influential nodes within the network.

$$\boldsymbol{D_i^A} = \frac{\sum_{t \in N} \frac{D_t^A}{L_t}}{N} \quad (1)$$

Paper III & IV: What are the synergies and trade-offs between national AMR and SDG policy?

Case studies selection

We analyzed AMR and SDG national action plans (NAPs). From 134 AMR-NAPs available in the WHO library, only those written in English and developed after the 2015 launch of the Global Action Plan (GAP) were included, resulting in a final set of 85 documents. These documents were then matched with the respective national development plans (SDG-NAPs) that outline time-bound sustainability objectives. A systematic web search identified 72 countries with such plans, but only 54 met the inclusion criteria (written in English and issued after 2015) (**Figure 6**). To capture both geographically and economically representation, 10 countries from Africa and Asia were purposively selected: Ethiopia, Uganda, Rwanda, Zambia, Kenya (low- and middle-income), and Thailand, China, Philippines, Japan, and Saudi Arabia (middle- and high-income). Details on selection and the complete list of documents are provided in the supplementary materials (an interactive version is available online at https://gedb.shinyapps.io/sdg-amr-explorer).

Data analysis

Assessing the alignment between AMR and SDG policies

To ensure methodological consistency and enable cross-contextual comparison, the analysis began with an examination of the alignment of goals and targets defined in the GAP-AMR and UN-SDG documents, which served as a blueprint. These objectives and targets were subsequently mapped onto identified AMR drivers, under the assumption that the achievement of the policy as outlined in the agendas would contribute to addressing the drivers. Next, we quantified the degree of overlap between each GAP-AMR objective and corresponding SDG using the Jaccard similarity coefficient (127). The overlap index, denoted as $J(AMR_i, SDG_j)$, represents the ratio of shared drivers to the total set of unique drivers across both agendas, as specified in formula (2). This international-level assessment informed the subsequent analysis of ten case-study countries.

$$J(AMR_i, SDG_j) = \frac{AMR_i \cap SDG_j}{AMR_i \cup SDG_j} \quad (2)$$

All analyses were conducted in R (v 4.3.3). To assess factors associated with the coverage of AMR drivers in national policy agendas, mixed logistic regression models were fitted, with country and continent specified as random effects. Additional subgroup analyses stratified by income level were performed to explore whether differences existed in the prioritization of actions

addressing AMR drivers under AMR-NAPs and SDG-NAPs across varying socio-economic contexts.

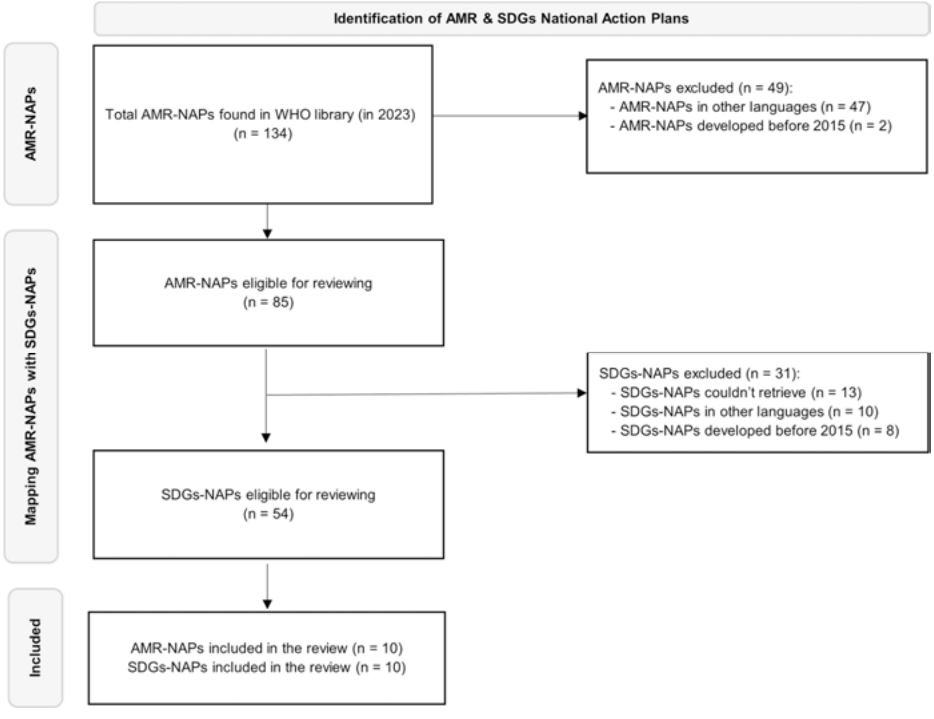

Figure 6. Flowchart of country and document selection for review.

Assessing the synergies and trade-offs between AMR and SDG policies

An AMR driver may be addressed simultaneously by multiple objectives within a single policy framework or across different policy agendas, for example, intensive forms of animal agriculture (including AMU) are shared drivers of both climate change (via greenhouse gas emissions) and AMR (128). Thispotentially leading to outcomes that are synergistic, conflicting, or independent. Such interactions can arise at different stages of the policy process. At the objective level, they emerge during the formulation of high-level goals and targets, which set the overall direction of action. At the implementation level, interactions are reflected in the design and execution of concrete actions and interventions, where practical measures may reinforce, counteract, or remain independent of one another. Importantly, these dynamics can occur within a single policy domain (intra-policy interactions) as well as between policy domains (inter-policy interactions) (129,130) (**Figure 7**), for example:

- *AMR-AMR policy interaction*: The inherent access-excess conflict between antibiotic use and resistance development where efforts to ensure

responsible use can restrict access in settings with high disease burden, where access to antibiotics is most needed.

- *AMR-SDG policy interaction*: SDG policies (SDG 2 & SDG 8) that aim to increase productivity and food security may increase animal stocking densities and antibiotic use, whereas AMR policy may address food security by reducing animal density and promoting ecological intensification strategies (e.g., biological control in crop agriculture, microbially enhanced immunocompetence in livestock).
- *AMR-SDG policy interaction*: Goals to promote responsible production and consumption (SDG 12), access to clean water (SDG 6) and human health (SDG 3) must be considered simultaneously, as waste from pharmaceutical manufacturing and healthcare sector sites can create resistance hotspots, especially where wastewater treatment, regulations and resources are lacking.
- *SDG-SDG policy interaction*: The economic incentives of the pharmaceutical industry to develop new antibiotics (SDG 12) may diverge from public-health needs (SDG 3) when profitability is lower than for chronic-disease drugs and the need to limit use of new antibiotics.

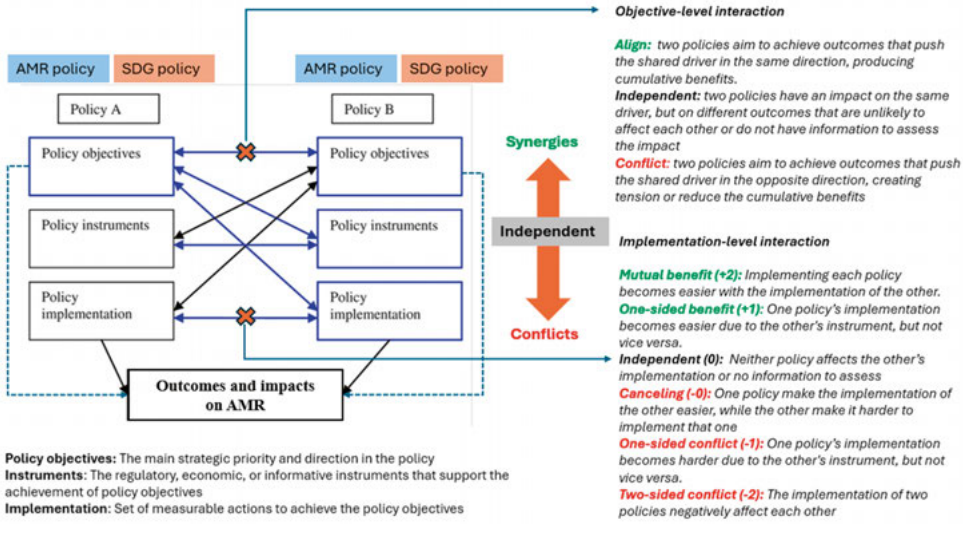

Figure 7. Conceptual framework illustrating interactions between AMR and SDG policies at both the objective and implementation levels. Adapted from Nilsson *et al.* (130).

Use of large language models for policy-interaction evaluation

The evaluation of policy interdependencies was facilitated using the advanced reasoning Large Language Model (*OpenAI o4-mini-high*) via an Application Programming Interface (API). The o4-mini-high language model was chosen as it demonstrated significant capabilities in understanding context, integrating extensive domain knowledge, and evaluating nuanced interactions. Half of the output produced by LLM were then compared with human review as a

gold standard to assess how well the LLM classifier agrees with human annotators. To evaluate the reliability of the large language model's classifications, we conducted five independent runs of the same policy interaction classification task. For each unique pair of policies, we compared the outputs across runs and calculated a Consistency Index, defined as the proportion of classifications that were identical to the most frequently assigned category. This metric ranges from 0 (no agreement across runs) to 1 (perfect agreement) and was computed separately for both policy objectives and policy implementation levels. The result shows that LLM has a high consistency in the classification task (**Figure 8**).

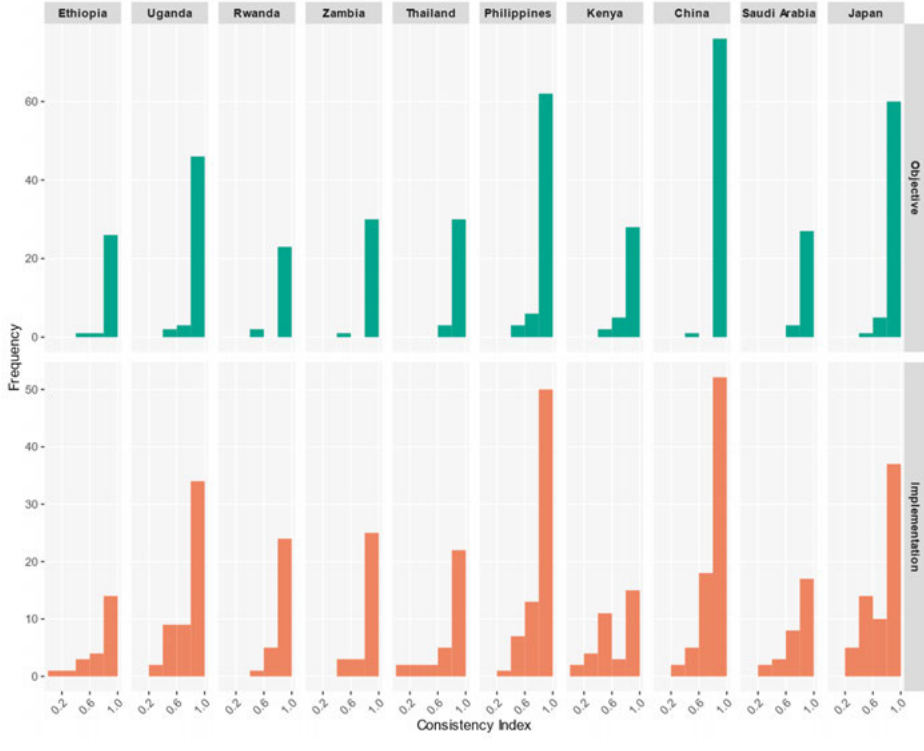

Figure 8. Distribution of consistency in results produced by LLM

Result

Paper I: Association between national action and trends in antibiotic resistance from 2000 to 2023

Ambitious government action can help reverse trends in AMR indicators between 2000 and 2016

Trend in AMR indicators exhibits a mixed pattern. Health system drivers decline over time between 2000 and 2016 (linear trend = -0.126 ± 0.017, $p<0.001$, categorical trend = 6/73 countries increasing, $p<0.001$), whereas both antibiotics use (linear trend = 0.289 ± 0.048, $p<0.001$, categorical trend = 55/65, $p<0.001$) and drug resistance index increase (linear trend = 0.184 ± 0.065, $p=0.01$, categorical trend = 21/25, $p = 0.002$). A non-significant trends is observed in AMR (linear trend = 0.019 ± 0.069, p = 0.8, categorical trend = 16/32, p = 1). However, our findings indicate that stronger level of national action in 2016 are consistently associated with improvements across all AMR indicator groups during 2000-2016. The overall action index is not correlated with the baseline state of the indicators but shows stronger association with reduction in AMR indicators rather than its individual components. Among the subcomponents, the Monitoring and Surveillance domain of the action index is most commonly associated with AMR indicators (significant in two of four indicators in both model types) while Prevention component is not associated with any indicators.

Figure 9 illustrates the ease of implementation to reverse trend in AMR indicators. For DRI and ABU, stronger action is needed (approximately 3.5–3.6 out of 4) for a 50% probability of indicator reductio. DRI shows almost no improvement below a score of 2, but the probability of progress increases sharply once action exceeds score of 3.5. ABU was somewhat more responsive, with a 25% reduction possible at score of 2.5 and about 50% at score of 3.5. In contrast, AMR requires less effort: a 30% chance of reduction is observed at score of 1.5 and 50% at score of 2.5. Drivers show overall high probabilities of improvement irrespective of action, but with a slight negative trend as action increases.

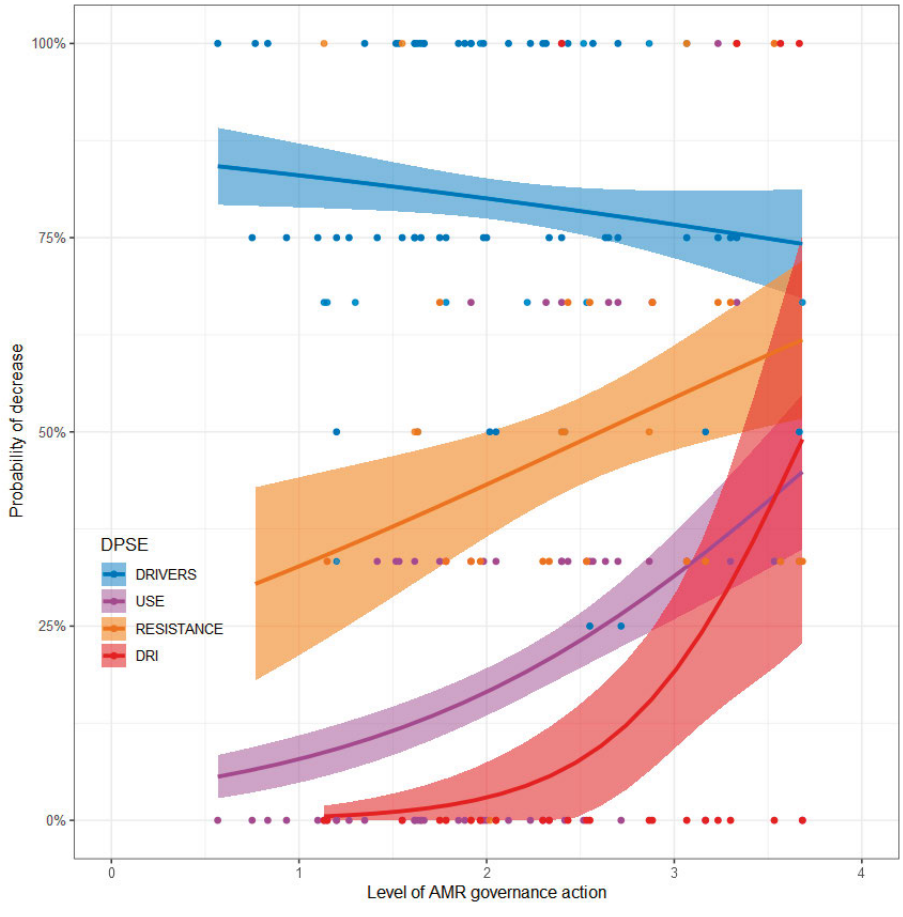

Figure 9. Proportion of declining indicators as a function of the action index. Shown is the proportion of lower-level indicators within a category that have witnessed a reduction from 2000 to 2016. Weight refers to the proportion of variables available for a given country. Uncertainty bands indicate standard errors. *Figure reproduced from the published manuscript.*

Most countries increased AMR governance between 2016 and 2023, though some reduced ambition

Our results also show that most countries surveyed have heighten their level of action in 2023 compared to 2016–17 (**Figure 10**). Approximately 70% of high-income countries (HICs) show progress, with the national governance action score rising from 2.43 to 2.92, while 83% of low- and middle-income countries (LMICs) also strengthen their response, with scores increasing from 1.62 to 2.06. However, progress was not universal: nearly one-quarter of countries reduce their level of ambition over the same period (30% of HICs and 17% of LMICs).

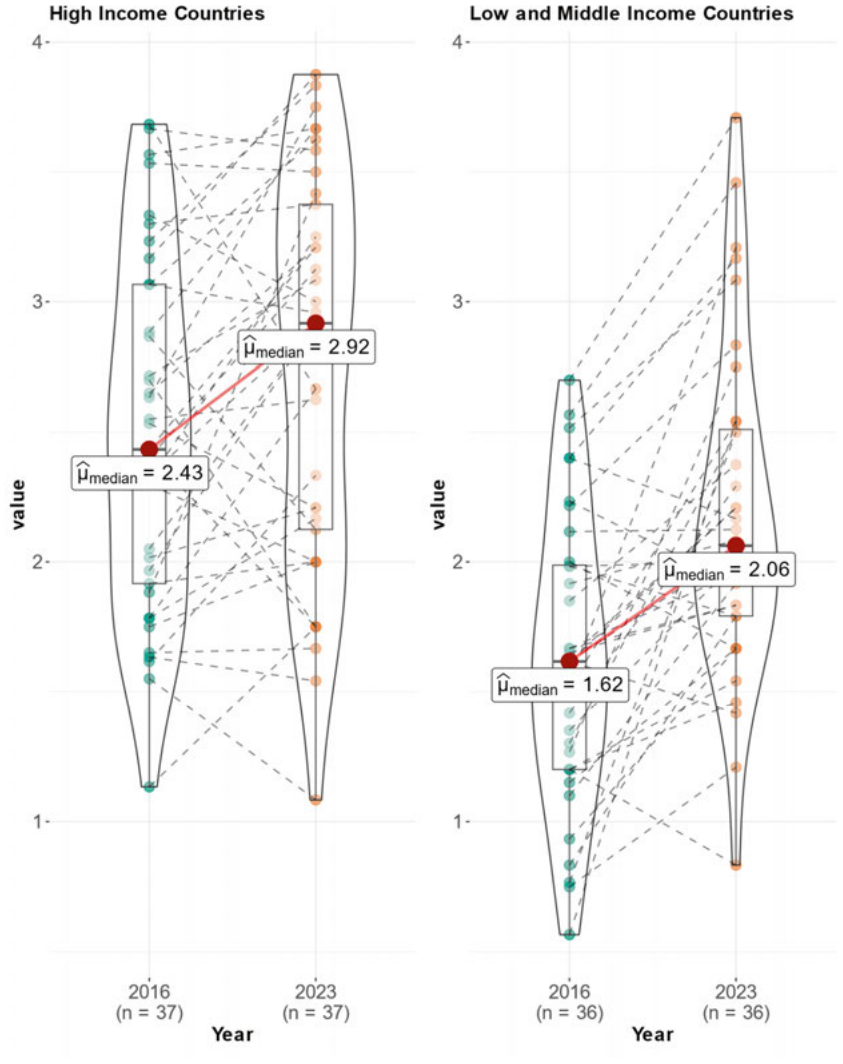

Figure 10. Changes in action index between 2016 and 2023

When comparing trends in national governance action with AMR indicators, distinct patterns emerge across indicator categories and income groups. For drivers, more than half of both HICs and LMICs exhibit a positive cycle, characterized by improved conditions accompanied by increased policy ambition. However, this proportion drops markedly for ABU, ABR, and DRI. Among LMICs, only 3 of 31 countries (10%) show a positive cycle for ABU, while 6 countries fall into a negative cycle The majority (around 70%) are "meeting the challenge," reflecting rising antibiotic use alongside stronger policy responses. For HICs, negative cycles are relatively common for ABU (24%, n = 34) and DRI (32%, n = 22), whereas positive cycles are rare, observed in only 5% of countries (n = 22) for DRI.

Paper II: Understanding the dynamics and role of drivers of antimicrobial resistance

Evidence bias about distal drivers of AMR identified in the literature

The study identified 2384 quotations in which causality relationships between AMR indicators were mentioned. From these, 217 unique causal links were retained, and a causal network of AMR was subsequently constructed (**Figure 12**). Using quartile rankings of the distalness index (D_i), the drivers were categorized into proximal drivers and distal drivers. Evidence involving distal drivers is more fragmented than that for proximal drivers. The number of review articles mentioning distal drivers is fewer on average (mean = 11.6, SD = 8.3) compared with those mentioning proximal drivers (mean = 14.6, SD = 8.1) (**Figure 11A**). Moreover, characterizing the full causal pathway from a driver to AMR requires a larger set of studies for distal drivers (mean = 2.0, SD = 0.7) than for proximal drivers (mean = 1.4, SD = 0.3), a difference that is statistically significant (Wilcoxon rank-sum test, $p<0.05$) (**Figure 11B**). The strength of evidence about distal drivers also tends to be weaker compared to proximal drivers (**Figure 11C**).

In addition, the study's findings show that most proximal drivers are found to be associated with containment (D_i = 0.49, SD = 0.14), access (D_i = 0.57, SD = 0.09), and conservation (D_i = 0.58, SD = 0.2) governance challenges. These include drivers related to the transmission of resistant bacterial infection in humans and animals, access to healthcare and quality antibiotics, patient and prescriber factors, economic incentives for prescribing antibiotics and the discharge of waste containing antibiotic residue from anthropogenic activities.

On the other hand, drivers associated with innovation (D_i = 0.62, SD = 0.07), infection prevention (D_i = 0.67, SD = 0.14) and surveillance (D_i = 0.69, SD = 0.16) governance challenges have mean distalness index values close to the grand mean, suggesting that they are intermediate causes of AMR. Finally, our analysis indicates that drivers related to multiple governance challenges (D_i = 0.83, SD = 0.12) are distal drivers. These often encompass societal development and governance factors, including substandard healthcare provision, gaps in policy adoption, implementation, and enforcement; crisis events; leadership and governance capacity; population growth and urbanization; and country development status.

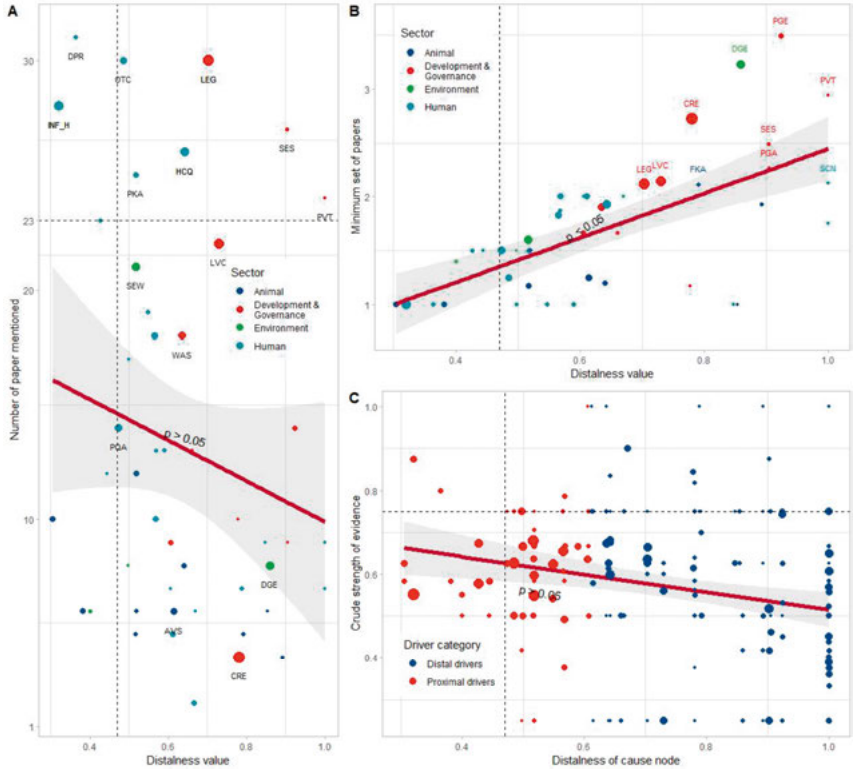

Figure 11. Evidence bias about distal drivers of AMR is identified in the literature. (A) Scatter plot showing driver distalness index (Di) against the number of identified reviews mentioning that driver. **(B)** Distalness index against the average minimum set of papers to describe the causal pathway from a node to AMR. Nodes are characterized according to sector. Node size represents for betweenness centrality index. **(C)** Distalness of cause node against average crude strength of evidence. Node size represents the frequency of mention of a causal relationship. *Figure reproduced from the published manuscript.*

Network analysis reveals key drivers for AMR intervention

Nodes with high centrality values indicate the intersection of several pathways; in other words, AMR is more likely to occur in the presence of these nodes. These nodes might be important for management since they connect different pathways. Our analysis reveals that contextual factors such as access to sanitation infrastructure; local living conditions; gaps in policy adoption, implementation, and enforcement; and crisis events are distal drivers with high betweenness and eigenvector centrality values. These drivers act as bridges that influence multiple parts of the AMR system. Interestingly, a country's level of development, population growth and urbanization emerge as distal drivers with low betweenness centrality values but high eigenvector centrality values, suggesting that while they do not directly link many causal

chains, they remain structurally influential across the wider network. Core–periphery analysis further reinforces the importance of access to water, sanitation and hygiene infrastructure (WAS), country development status (PVT), gaps in policy adoption, implementation and enforcement (LEG), substandard healthcare provision (HCQ), and population growth and urbanization (PGE) as key distal drivers. Crisis events (CRE), though rarely cited directly, appear to amplify AMR by disrupting health systems and increasing infection risks (**Figure 12**). Unsurprisingly, key proximal drivers, including risks of infection in humans (INF_H), patient knowledge and attitudes (PKA), inappropriate prescribing behavior of doctor (DPR), and ease of access to over-the-counter antibiotics (OTC), are the most frequently identified in the literature.

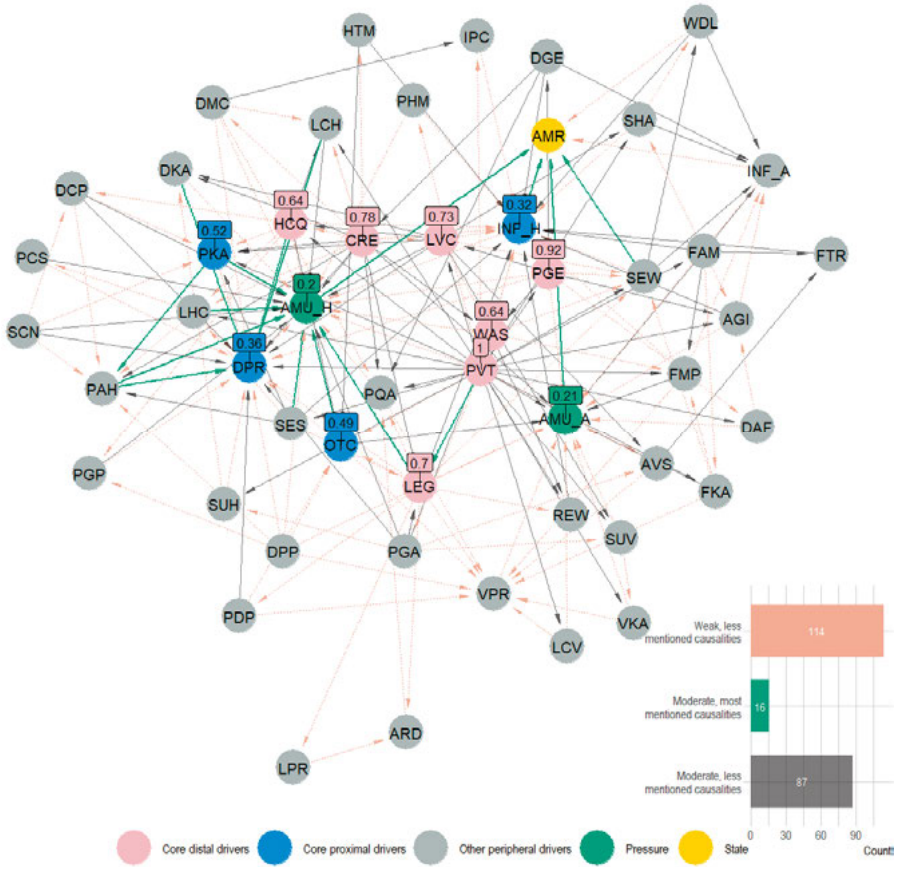

Figure 12. AMR core-periphery network structure. The core group consists of highly connected and central nodes, while the periphery group includes nodes that are less connected and less central to the network. Edge colors represent strength of causality and frequency of mention in the literature. *Figure reproduced from the published manuscript.*

Paper III + IV: Interactions between AMR and SDG policies

Coverage of AMR drivers in AMR and SDG agendas

Analysis of overlaps between GAP-AMR objectives and UN-SDG targets reveals varying degrees of alignment. GAP-AMR Objective 1 (awareness) aligns most with SDGs 2 and 6 (13% each), while Objective 2 (surveillance) strongly overlaps with SDG 3 (38%). Objective 3 (infection prevention) is moderately linked to SDGs 3, 6, 9, and 11, reflecting the role of water, sanitation, and infrastructure. Objective 4 (responsible use) shows moderate overlap with SDGs 3, 6, and 9, whereas Objective 5 (sustainable investment) aligns strongly with SDGs 8, 9, and 16 (**Figure 13**).

Figure 13. Overlap between the AMR and SDG policy in the international agenda. Each cell in the heatmap represents a calculated overlap score (range from 0 to 1) between AMR and SDG objectives. *Figure reproduced from the published manuscript.*

A mixed Poisson regression model is employed to explore factors influencing how often drivers are targeted in policy documents. Overall, AMR drivers are less frequently targeted by the SDG agenda than by the GAP-AMR (IRR=0.59, *p=0.002*). Distal drivers are also less targeted than proximal ones (IRR=0.63, p=*0.073*), but a significant interaction (IRR=2.78, *p<0.001*) indicates that distal drivers are more often addressed through the SDG framework, particularly those linked to poverty, crises, and socioeconomic factors.

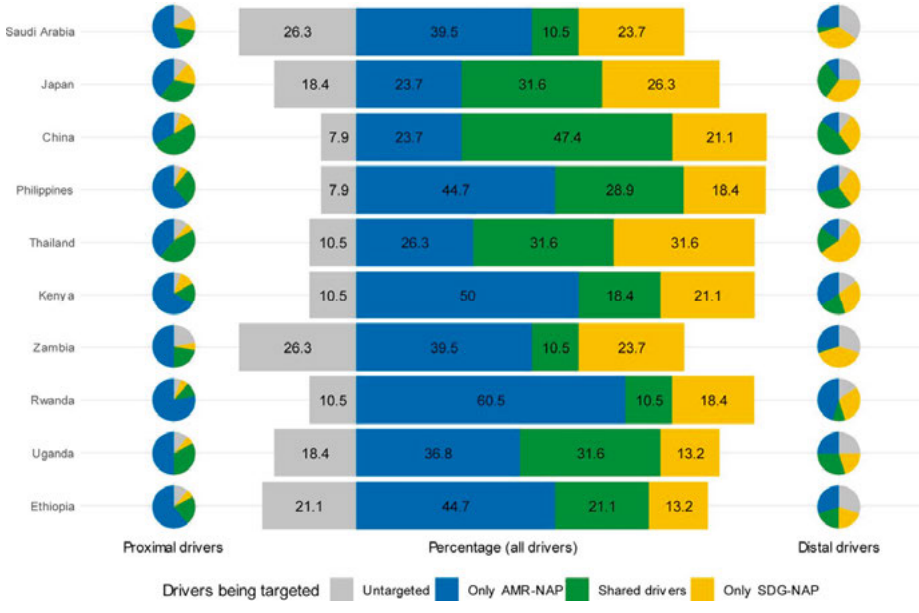

Figure 14. Coverage of AMR drivers in national policy agendas *Figure reproduced from the published manuscript.*

In national policies, proximal drivers are the main focus of AMR-NAPs, with coverage between 72–89%. The overlap between AMR-NAPs and SDG-NAPs is generally lower than at the international level, ranging from 11% in Rwanda to 50% in China. China, Thailand, Japan, and Uganda show moderate overlaps (33–50%), while other countries fall below 30%. Proximal driver coverage in SDG-NAPs is generally higher in Asia than in Africa, although 6–22% of proximal drivers remain unaddressed by any national policy (**Figure 14**). Distal drivers received less attention in AMR-NAPs (30–60% coverage) but are more often targeted through SDG-NAPs (20–55%). The overlap between AMR- and SDG-NAPs for distal drivers is lower than for proximal ones, ranging from none in Zambia to 45% in China. Again, China, Thailand, Japan, and Uganda show higher overlaps. However, a greater proportion of distal drivers (10–35%) remains uncovered by any national policy compared to proximal drivers (**Figure 14**).

Synergies and trade-offs between AMR and SDGs policies at the national level

Coherence among national AMR-related policies is assessed by comparing whether actions targeted at the same driver operate synergistically or in conflict, both within each agenda (AMR–AMR and SDG–SDG) and across agendas (AMR–SDG). **Figure 15** illustrates the distribution of these policy interactions across the countries studied. At the objective level, most national strategies are found to be internally coherent. Nearly all countries demonstrate full alignment among AMR policy objectives, with the exception of Rwanda (87.5%). AMR–SDG alignment is also high, ranging from 70% (Ethiopia) to 100% (China, Rwanda). Likewise, SDG–SDG interactions show strong internal consistency, scoring between 92% (Japan) and 100% in several cases. However, when moving from policy objectives to implementation, variability increases, revealing a growing gap between policy intent and practice. While AMR policies generally retain high internal coherence, Kenya and Thailand drop to 66.7% alignment. Cross-sector coherence between AMR and SDG implementation declines more sharply, particularly in Ethiopia (62.5%) and Thailand (75%), suggesting that operational measures do not always reflect stated strategic priorities.

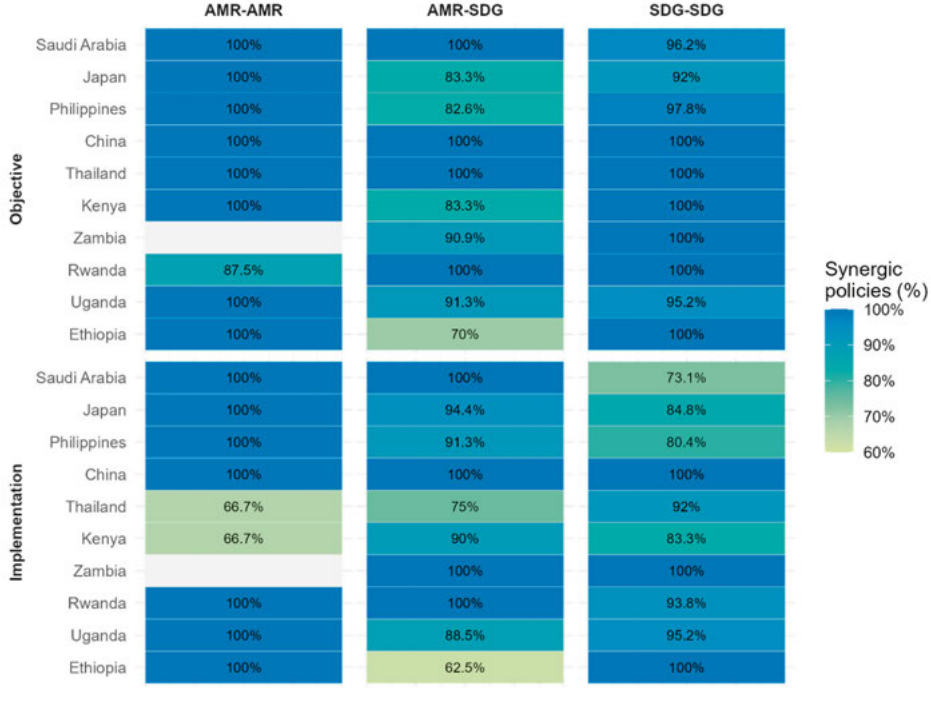

Figure 15. Distribution of objective interaction by country and policy

Philippines (AMR–SDG objective independence example)

- **AMR Objective (AMR-02):** Strengthen surveillance and diagnostic capacity in hospitals and environmental labs and build workforce competencies for AMR monitoring and ensure proper disposal of hazardous waste, through lab assessments, environmental residue monitoring, and implementation of waste-handling protocols.
- **SDG Objective (SDG-09):** Revitalize industry by amending the Renewable Energy Act and the Electric Power Industry Reform Act to lower energy costs, promote renewables, and ensure reliable power supply.

Interpretation: While AMR-02 aims to address the environmental degradation via diagnostics, surveillance, and waste-management measures, SDG-09 focuses exclusively on energy-sector regulation that facilitate renewable energy adoption and lower energy costs. Although renewable energy can contribute to reduced environmental degradation, the policy objectives do not explicitly target environmental contamination in the same direct manner, resulting in an independent relationship.

Kenya (AMR–SDG objective independence example)

- **AMR Objective (AMR-03):** Roll out the National Infection Prevention & Control Strategy by developing and enforcing IPC policies and standards. Embed IPC into continuing professional development and in-service training for all healthcare workers. Promote hand hygiene, train staff via online courses, and strengthen accreditation/quality-assurance standards to ensure timely reporting and prevention of healthcare-associated infections.
- **SDG Objective (SDG-03):** Prevent and reduce HIV infections through expanded prevention of mother-to-child transmission services.

Interpretation: Although both policies center on infection control in human health, AMR-03 is exclusively focused on curbing healthcare-associated resistant bacteria through IPC measures, while SDG-03 is dedicated to HIV prevention and transmission elimination. Their goals operate on different pathogens, populations, and intervention frameworks, so they do not directly reinforce or conflict, and are therefore independent with respect to AMR drivers.

Zambia (AMR–SDG objective independence – implementation mutual benefit example)

- **AMR Objective (AMR-03):** Strengthen sanitation, hygiene and biosecurity in animal/plant health – e.g. improving livestock/plant censuses, mapping biosecurity points, and reinforcing checkpoints and barriers to reduce infections.

- **SDG Objective (SDG-02):** Accelerate agricultural industrialization and diversification – e.g. expanding mechanized "farm blocks," boosting crop and livestock production, and scaling up fisheries to drive economic growth.

Interpretation: AMR-03's objective is to reduce infection incidence through enhanced sanitation, hygiene and biosecurity, whereas SDG-02's objective is to boost agricultural and livestock production and productivity. These strategic priorities are distinct and neither clearly reinforces nor directly opposes the other in terms of their stated outcomes. However, at the implementation level, SDG-02 roll-out of community livestock service centers, veterinary laboratories and devolved veterinary services builds surveillance, diagnostic and extension capacity that directly supports AMR-03's requirements for livestock/plant census, mapping and biosecurity checkpoint enforcement. Conversely, AMR-03's strengthened biosecurity checkpoints and data systems help safeguard animal health and protect the production gains sought under SDG-02.

The interaction matrix (**Figure 16**) summarizes how AMR and SDG policy agendas intersect, showing objective-level relationships in the upper triangle and implementation-level relationships in the lower triangle. At the objective level, AMR goals show strong internal coherence, with nearly all policy interactions classified as synergistic. A similar pattern is seen within the SDG goals, where most objectives aimed to target AMR drivers are formulated to be aligned. Prominent synergies are observed between efforts to improve water and sanitation (SDG-06), promote urban development (SDG-11) and responsible production and consumption (SDG-12). Yet, several areas of tension emerge, particularly around food security and agricultural productivity (SDG-02). Actions under this goal often generate both synergy and trade-offs, for instance supporting economic growth (SDG 8) and reducing inequalities (SDG 10) on one hand, but sometimes conflicting with sustainable consumption (SDG 12) and environmental protection on the other. Similar trade-offs appear between policies promoting industrial development (SDG-09) and those aimed at urbanization or ensuring sustainable production systems (SDG-11 and SDG-12). These tensions highlight the persistent challenge of balancing economic growth with environmental and social sustainability.

In contrast, the links between AMR objectives and the broader sustainable development agenda reveal a more heterogeneous pattern. A clear example of synergy appears where improving access to clean water and sanitation (SDG-06) directly supports the goal of reducing infections and slowing the spread of resistance (AMR-03). However, other domains such as food security, health, urban development, and responsible consumption exhibit mixed or conflicting outcomes. For instance, policies promoting agricultural intensification (SDG-02) may inadvertently increase antimicrobial use, undermining AMR awareness and stewardship (AMR-01, AMR-04). Likewise, the pursuit

of rapid economic growth (SDG-08) can conflict with the AMR objective on sustainable investment (AMR-05) if growth incentives encourage excessive antimicrobial use or weaken regulatory controls.

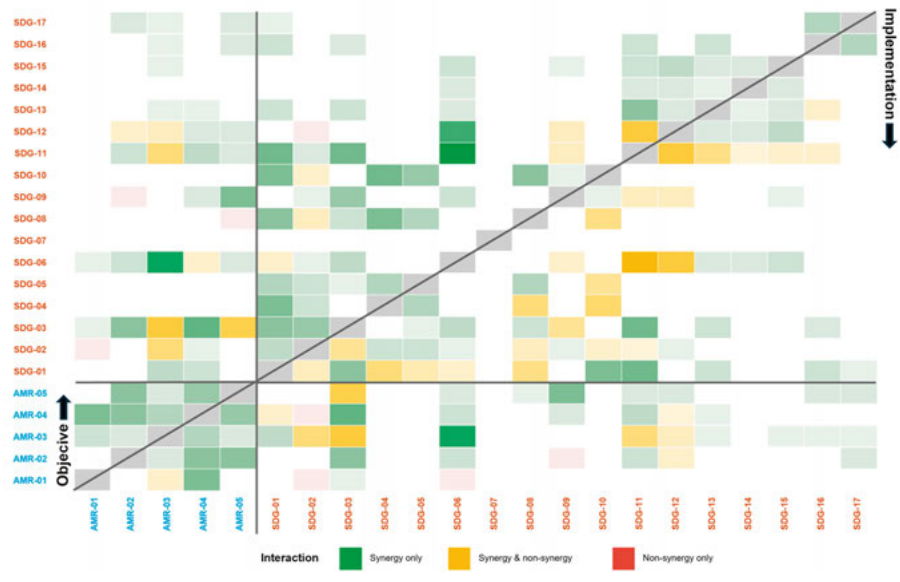

Figure 16. Interaction Matrix of AMR and SDG Policy Agendas. The matrix shows interactions between 05 AMR objectives and 17 SDG policy SDGs. The upper triangle illustrates policy objective interactions; the lower triangle illustrates policy implementation interactions. Cell transparency represents the frequency of policy interactions.

At the implementation level, where high-level goals are translated into concrete actions, the relationships between AMR and SDG agendas become more fragmented and less consistent than at the objective level. Within AMR, most actions continue to reinforce one another, although a rare case of both synergy and trade-off appears between efforts to reduce infections (AMR-03) and raise awareness (AMR-01). For SDG-SDG interactions, inconsistencies are more frequent than at the objective level. Actions addressing socio-economic drivers such as poverty, hunger, education, and gender equality often show a mix of synergy and non-synergy outcomes. Similarly, policies advancing urban development tend to align poorly when pursued without sufficient consideration of environmental priorities, including sustainable consumption (SDG-12), climate action (SDG-13), and ecosystem protection (SDG-14, SDG-15). Notably, the interactions between AMR and SDG implementation show more non-synergy policy interaction. Trade-offs are also more evident at this level. Mixed and conflicting outcomes are most frequently observed in the interactions between food security (SDG-02) and AMR objectives on awareness (AMR-01) and antimicrobial use (AMR-04), as well as between WASH objective (SDG-06), industrial development (SDG-09), and sustainable production (SDG-12) with different AMR priorities.

Discussion

The aim of this thesis is to improve understanding of the drivers that underpin the emergence and global spread of AMR, thereby informing policy design that addresses these drivers through both AMR-specific measures and alignment with the 2030 agenda. Prior to this work, the literature provides limited insight into how AMR drivers shape resistance patterns and how they are addressed within AMR and SDG policy agendas.

Empirically, the thesis provides cross-national evidence on the association between AMR-specific national action and temporal trends in key indicators across 73 countries, covering drivers, pressures, state, and exposure. It demonstrates that stronger governance action correlates with improvements across AMR indicators and introduces the concept of *governance syndrome* as an intuitive framework for assessing national progress. In addition, the thesis constructs an empirically grounded causal network of AMR drivers from an umbrella review and introduces the driver distalness index, which is proposed as an analytical lens for comparing causal proximity, leverage potential, and evidence strength across drivers, clarifying why upstream conditions often determine the effectiveness of downstream stewardship. Further, by analyzing AMR and SDG national action plans across 10 countries in Africa and Asia, the thesis quantifies the alignment between both policy agendas, showing that coherence observed at the objective level often weakens during implementation, especially where economic and environmental goals intersect. Conceptually, the work advances the study of policy coherence and interaction between AMR and SDG agendas, providing a transferable analytical framework to assess alignment across objectives and implementation.

In sum, this thesis has several implications. It provides a foundation for developing theories and testing hypotheses on how integrated AMR policies targeting multiple proximal and distal drivers can be effectively designed and evaluated. Furthermore, it also provides empirical evidence for policymakers, emphasizing the need to strengthen cross-sectoral governance mechanisms and to enhance coherence between health, agricultural, and environmental policies in order to maximize synergies and minimize trade-offs.

Progress achieved, challenges remaining. Why global action still falls short in combating AMR?

Analysis of long-term associations between AMR indicators and governance actions allows us to conclude that the estimated levels of intervention required to reverse trends in AMR are likely to be effective, and that reductions might be achievable at lower action. The key unknown is the time required for these effects to become visible and, perhaps more importantly, for how long such reductions can be continued (131). The classification of countries into governance syndromes reinforces this conclusion by demonstrating how differences in institutional commitment, regulatory strength, and policy coherence translate into divergent outcomes. Experiences from the Nordic countries fighting with AMR exemplifies the case. These countries established comprehensive national AMR surveillance systems and stewardship programs as early as the 1980s and 1990s (132). Over three decades of sustained investment in monitoring, regulation of antimicrobial use, and intersectoral collaboration have contributed to stabilizing, and in some instances reducing, AMR burdens. Yet, despite recent intensification of efforts, countries such as the Netherlands and the United Kingdom, both of which demonstrated high levels of action and notable policy expansion between 2016 and 2023, remain classified within a negative cycle for AMU. This divergence underscores that resilience against AMR is not built solely through the intensity of interventions but also through their consistency and institutional embedding over time.

Of note, this finding should also be interpreted in light of temporal dynamics. Trends observed up to the 2016–17 survey may underestimate the true impact of policy change, as interventions adopted shortly before this period would not yet have influenced outcomes. By 2023, most countries had increased their level of action compared with 2016–17, but about one-quarter reduced their efforts. These declines may reflect shifting priorities, such as during and after the COVID-19 pandemic, or improved reporting accuracy in later TrACSS surveys. The latter could inflate the number of countries classified under “relaxed response” or “negative cycle,” complicating governance assessments.

Among the indicators, reductions in drug-resistant infections (DRI) are the most difficult to achieve, followed by reductions in AMU and AMR. The difficulty of reversing downstream indicators may imply that cross-sector coordination and longer time horizons are required for upstream interventions to be effective. This hierarchy is consistent with earlier research showing that stewardship interventions can modify prescribing practices in the short term but often struggle to reverse entrenched resistance profiles, particularly when resistant strains are already widespread (39,88). The linear trend in ABR shows fairly weak correlation with action, whereas the categorical trend is consistently correlated. The former pattern could be an indication of (1) a non-

linear association between action and ABR; (2) that bacteria targeted for management vary by country and potentially go beyond the three indicators available for this analysis, or; (3) that absolute rates of resistance can be circumvented through various strategies. The latter pattern could indicate a threshold of action above which such reductions are more likely to be achieved.

By contrast, national action on AMR has a fairly small effect size on the linear trend in health system drivers. Several explanations are possible. First, action on drivers might be very similar across and between countries, independent of national AMR action. The weak or, in some cases, negative association between AMR-focused action and these system drivers may reflect a "ceiling effect" in high-income countries, where access to essential services is already near universal, leaving little room for measurable gains. More likely, however, the limited effect stems from the fact that distal drivers are only addressed to a small degree by current AMR policies and interventions, and instead by actions coordinated under other policy frameworks. For example, structural improvements in sanitation, vaccination, and workforce capacity are primarily shaped by wider health and development policies rather than AMR-specific interventions. In order to observe a significant reduction in drivers, strategies must therefore be context-sensitive, multi-pronged and coordinated across policy domains. Linking AMR interventions with broader agendas on sustainable development is essential; otherwise, national AMR strategies risk being confined to short-term containment, while the structural conditions that perpetuate resistance remain unresolved (30).

Distal drivers as leverage points: Aligning societal development trajectories with AMR mitigation

In settings where AMR is already widespread and the capacity for mitigation is constrained, incremental approaches are simply insufficient. Instead, addressing AMR requires fundamental transformation of the broader social-ecological system, with greater emphasis on the upstream drivers that shape patterns of infection, antimicrobial demand, and selection pressure. This thesis advances understanding of AMR as a complex system by mapping how its drivers interconnect, moving beyond the traditional focus on individual-level risk factors (92,133) to a systems perspective in which institutional, infrastructural, economic, and cultural conditions configure the opportunities and incentives to use antimicrobials.

Evidence for distal drivers found in the literature tend to be more fragmented than for proximal drivers, as in line with those of previous studies (134,135). There are still major research gaps that impede our efforts to understand AMR drivers; thus it is likely that distal drivers are currently underreported in the literature. This may be due to, first, the absence of existing

framework to distinguish proximal from distal drivers, combined with the heterogeneity of terms used to describe them, and the identification of distal drivers can be challenging due to heterogeneity in the form and granularity of language. Second, empirical data remain limited for certain distal drivers, such as the impacts of crisis events, climate change and reduced biodiversity, and corruption, whose influences are typically diffuse and mediated through multiple causal pathways, thereby complicating efforts to establish causality, as well as measuring potential co-benefits of AMR-sensitive interventions on distal drivers across various settings (82).

The distinction between proximal and distal drivers has substantive implications on AMR policy. Recognizing these as distinct yet interconnected domains helps policymakers to identify leverage points and evaluate systemic impacts of interventions across the One Health contexts, thereby guiding the formulation of evidence-based targets and objectives in the national action plan (136–138). Proximal drivers, often associated to containment challenges (e.g., facility-level infection control), access issues (e.g., over-the-counter sales), and conservation challenges (e.g., prescribing practices), are amenable to targeted by AMR-specific measures, and often yield faster, visible outcomes. While such interventions can provide short-term benefits, they largely function as temporary fixes that manage system's symptoms rather than root causes, and their impact is continually undermined by persistent structural conditions fueled by distal drivers.

In fact, distal drivers (e.g., WASH deficits, health-system underfunding, livestock production incentives, weak regulatory capacity, education and norms) are systemic, cross-sectoral, and complex, requiring long-term planning and substantial investment in infrastructure, poverty alleviation, and food system reform. They often operate at higher levels of organization, and typically exhibit long and uncertain lag times to measurable effects (136,137) (**Figure 17**). Only by addressing these upstream drivers, societies can sustainably reduce the demand for antimicrobials, limit the opportunities for resistant strains to emerge, and slow the global spread of AMR. Otherwise, current efforts are unlikely to be sustainable, with LMICs carrying a heavier burden (82,139).

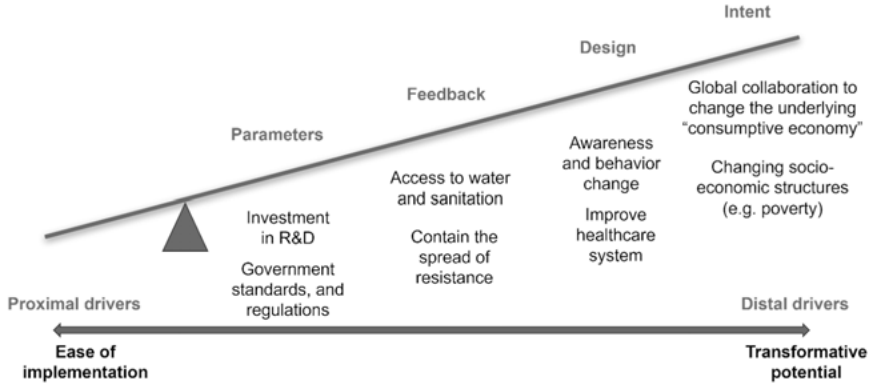

Figure 17. Illustration of potential transformation of interventions addressing drivers of AMR. *Interventions can be implemented at various leverage points within the system. They include alteration of the system parameters (e.g., changing AMU practices), modification of feedback mechanisms (e.g., managing the increased demand for antimicrobials driven by infection rates), and the re-conceptualization of the system's design and underlying intent (e.g., restructuring the social and institutional frameworks governing the feedback loops and parameter settings).*

The second implication is that a focus on distal drivers compels the integration of AMR policies with broader sustainable development agendas (82). Viewing AMR through the lens of the sustainability science can open a door for meaningful integration of AMR governance, fundamentally shifting the focus from reactive measures (managing resistance after it emerges) to proactive, preventative strategies (creating societies where infections are less common and antimicrobials are less needed) (140,141). This raises a critical question: how can societies achieve health, poverty reduction, food security, and economic growth within a "Safe and Just Operating Space" that prevents AMR from surpassing ecological limits? (**Figure 18**).

Meeting this challenge requires building resilience across multiple levels of the AMR causal chain, with particular emphasis on driver resilience, which targets the distal ecological, economic, and social determinants that shape patterns of infection and demand for antibiotics. (97,133,142). Tackling shortfalls in access to essential social services, especially among underserved populations, is central to this effort. Initiatives aimed at lifting people out of poverty, improving education, and expanding access to public health interventions such as water, sanitation and hygiene (WASH), vaccination have demonstrated significant success in reducing infectious disease incidence and prevalence (142). By setting the overall direction for societal development, actions taken to meet health and equity targets set as part of the global SDG agenda could have just as large impact on AMR as those actions within the AMR-specific agenda (30,97).

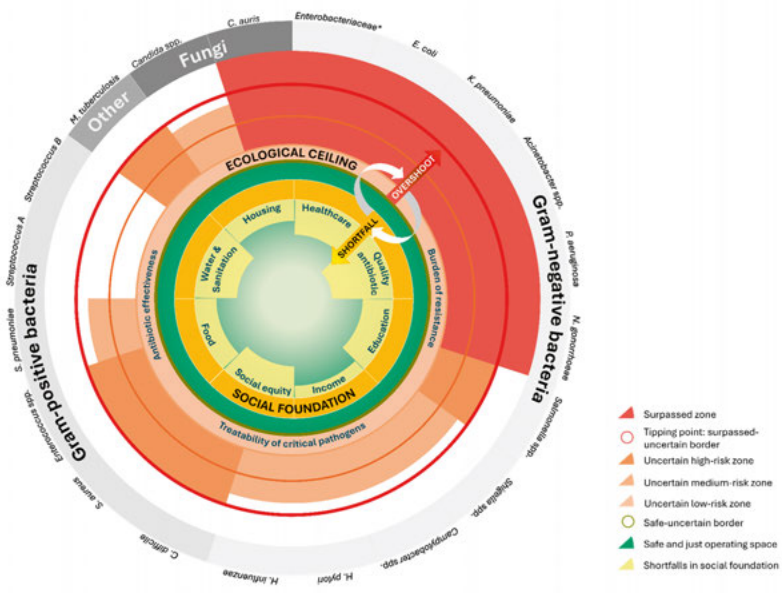

Figure 18. Illustration of the Safe and Just Operating Space for AMR, constituted by the bio-ecological ceiling and social foundation dimension. Abbreviation: Acinetoba= *Acinetobacter* genus; *C.difficile= Clostridioides difficile;* Campy= *Campylobacter* genus; *Candida= Candida* genus except *Candida auris; C.auris= Candida auris;* Enterobact= *Enterobacteriaceae* family except *Escherichia coli, Klebsiella pneumoniae* and genera *Salmonella* and *Shigella;* Enterococ= *Enterococcus* genus*; E.coli= Escherichia coli;* GAS= *Streptococcus* Group A; GBS= *Streptococcus* Group B; H.influen= *Haemophilus influenzae; H.pylori= Helicobacter pylori;* K.pneumo= *Klebsiella pneumoniae*; N.gono= *Neisseria gonorrhoeae;* P.aerugi= *Pseudomonas aeruginosa; Salmonella= Salmonella genus; Shigella= Shigella genus;* S.pneumo= *Streptococcus pneumoniae; S.aureus= Staphylococcus aureus;* TB= *Mycobacterium*.

Policy gaps in integrating SDGs into AMR planning and implementation

This thesis highlight a significant gap in the current AMR policy landscape, where the drivers of AMR are at risk of being redundantly addressed, narrowly focused or entirely overlooked by targeted AMR and SDG policies. Such gaps undermine the potential of integrated governance and may reduce the overall effectiveness of both AMR and sustainable development strategies.

On a positive note, drivers addressed by both the AMR and SDG-related policy agendas could be seen as encouraging, as they suggest progress towards policy integration. These overlaps suggest a growing recognition that AMR is not only a health issue but also an integral component of the SDG agenda. Policy integration increases the likelihood that interventions can

simultaneously advance SDG objectives while reducing the risks of AMR. However, this potential can only be realized if effective coordination between implementing bodies is ensured (120,143–145). Without institutionalized coordination, even well-aligned policies may operate in silos, duplicating efforts or working at cross-purposes, thereby limiting impact.

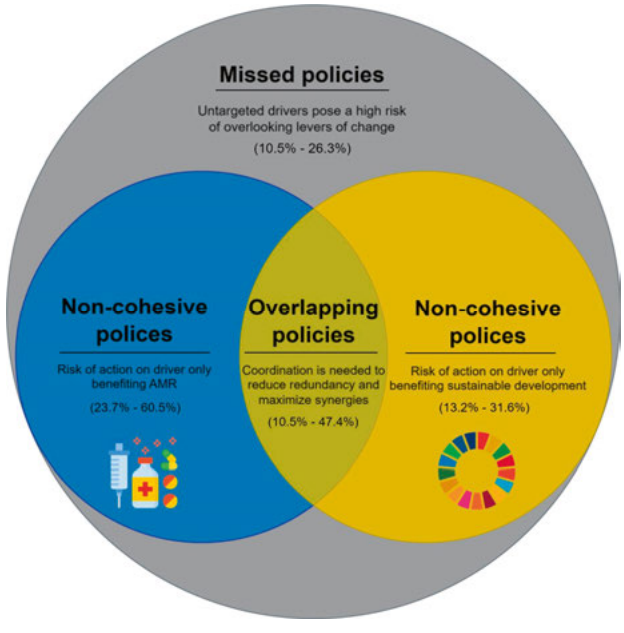

Figure 19. Policy gaps in integrating SDGs into AMR planning and implementation. *The Venn diagram illustrates three governance risks. Overlapping policies, where AMR drivers are targeted by both agendas, risk redundancy. Non-cohesive policies, where AMR drivers are acknowledged by only one framework, presenting a risk of only benefiting sustainable development or AMR at the expense of the other. The outer grey area highlights the risk of missed policies due to untargeted drivers, highlighting the risk of overlooking significant levers of change.*

Policies that address drivers targeted by only one agenda pose particular challenges. When actions are confined to AMR agendas, they may generate trade-offs for sustainable development. For example, a pathogen-centric approach that emphasizes biosecurity in animal health may reduce disease transmission but can also impose disproportionate economic burdens on smallholder farmers, thereby affecting livelihoods and equity (SDG 5, 8, 10) (146–148). Conversely, when drivers are addressed exclusively within SDG frameworks, they may advance development objectives but fail to adequately account for AMR consequences. For example, efforts to promote responsible consumption and production (SDG 12) align with antimicrobial stewardship in principle, but they can also generate short-term trade-offs in production systems and consumer behavior that complicate AMR mitigation (97).

A critical concern lies in the risk of overlooked levers of change, drivers of AMR that are not acknowledged by either AMR or SDG frameworks. These blind spots represent missed opportunities where potentially interventions are absent from policy discourse. One example is the role of global travel and migration in spreading resistant pathogens, which remains largely unacknowledged in both global AMR and SDG agendas. While some of these gaps may reflect challenges of feasibility or political sensitivity, they nonetheless point to the need for a more comprehensive mapping of AMR drivers across scales and sectors.

When examining overlapping policies between AMR and SDG, our analysis underlines that high-level alignment may not be sufficient. While many national policy texts show consistency at the objective level, the translation of these objectives into concrete implementation is uneven. In practice, operational measures often diverge, leading to limited or fragmented outcomes. The finding is in line with previous findings, where they indicate that although many governments acknowledge the importance of aligning AMR and SDGs policy frameworks, limited evidence exists on their practical integration within national contexts (90,149,150). Without dedicated financing, enforceable governance mechanisms, and strong political will, even well-aligned AMR and SDG objectives risk delivering only limited real-world impact.

Our findings also highlight clear areas of synergy and conflict policy. Synergistic policy interactions are often observed at the nexus of AMR objectives with core health and environmental goals, for example where AMR containment efforts align with good health and well-being (SDG-03), clean water and sanitation (SDG-06), or sustainable cities and communities (SDG-11). These are areas where advancing public health measures (like infection prevention and antimicrobial stewardship) simultaneously supports development targets – a natural synergy that policymakers can leverage (151).

By contrast, conflicts tend to emerge at the interface between AMR targets and economic or industrial development goals. In agriculture, for example, productivity-oriented policies under SDG 2 often promote intensive farming practices to meet food security and trade demands. While such strategies may boost short-term yields, they simultaneously increase antimicrobial use and environmental contamination, thereby undermining AMR containment efforts. Similar tensions arise in relation to industrial growth (SDG 9) and economic expansion (SDG 8), where the pursuit of competitiveness and innovation can deprioritize environmental safeguards, including wastewater treatment or pollution control (152–158).

Highlighting these nexus areas of synergy and conflict is important. It shows where co-benefits can be harnessed (as in health, sanitation, and environmental domains) and where careful balancing or innovation in policy design is needed to mitigate conflicts (as in the economic growth and industrial development domains). Tackling the complexity of AMR, therefore, requires breaking down the challenge into a set of policy areas that can be integrated

into existing governance mechanisms and accountability structures to ensures a more holistic and equitable approach. Policies that broadly address social problems, such as water and sanitation, are more preferable as they may be highly politically feasible across geopolitical contexts (159). Effective implementation of integrated policies will depend on national governments formulating and executing a coherent set of targets that concurrently address both agendas, thereby enhancing synergies and mitigating conflicts.

Limitations

This thesis has several limitations that should be acknowledged.
First, this thesis draws primarily on secondary datasets and document resources, which constrains its ability to observe how policies are implemented in practice and how decisions are made, negotiated, and adapted over time. Without direct engagement with policymakers, implementers, and affected communities, the analysis cannot fully capture implementation fidelity, informal practices, political incentives, budgetary constraints, or inter-ministerial coordination. Future work should therefore complement the secondary-data approach with mixed-method designs that include qualitative fieldwork, process and expenditure evaluation, policy network analysis, and co-production with stakeholders to validate findings and elucidate mechanisms.

Second, the analysis of national trends in AMR indicators and governance action is constrained by data availability and quality. Data coverage varies across indicator groups and is generally biased towards HICs. Moreover, the level of governance action is self-reported by countries, which may not accurately reflect the actual degree of policy implementation on the ground. Furthermore, the study cannot account for how long policies have been implemented. Countries with higher policy ambition may also be early adopters, meaning their policies have been in place longer and thus appear to have larger effects compared to countries that have only recently begun implementation. Additionally, the data used were restricted to antibiotic indicators in the human health sector, limiting the ability to draw conclusions about AMR drivers in agriculture, animal health, or environmental systems.

Third, while the network analysis used in study II provides insight into potential leverage points, it simplifies the complexity of real-world systems. High centrality does not necessarily equate to high policy leverage; interventions that appear influential in theory may be less effective in practice if local conditions, governance structures, or behavioral contexts are not considered. Moreover, many interventions targeting AMR drivers are often implemented at points far removed from where AMU and AMR are measured, making it difficult to trace causal pathways or anticipate unintended effects (160). Developing methods to link upstream interventions with downstream AMR outcomes should therefore be a central priority for the AMR research community.

Finally, the scope of the third and fourth studies is limited to a relatively small set of countries, which restricts the generalizability of findings. Although the case studies provide valuable insights, they cannot represent the full diversity of AMR governance challenges globally. The analysis is based on analyzing policy text rather than implementation or outcomes, so it cannot establish causal effects or verify whether stated synergies translate into practice. The use of a large language model introduces additional limitations. Models tend to have an optimism-bias, sometimes classifying policy

interaction as “aligned” based on semantic similarity. This can make policies from the same agenda policies look more coordinated than they really are, especially when the goals are broad or vague. In addition, analyses depend on publicly available national documents that may be incomplete, outdated, or silent on sub-national directives, and cross-country differences in terminology were not systematically accounted for.

Future perspectives

The work presented in this thesis highlights multiple perspectives for future research on the drivers of AMR and policy development to address them.

1) Bridging theoretical and empirical networks of AMR drivers

Findings from Study II indicate a bias in the existing evidence base, where distal drivers of AMR are substantially underrepresented in the literature. The driver network developed in this thesis provides a starting point to address this bias by providing a structured, empirically grounded framework that maps causal linkages and identifies potential leverage points across One Health domains. Future research can build on this framework by empirically validating the associations among drivers. This involves identifying measurable indicators for each driver and assessing the availability and consistency of time-series data to track their evolution. Once such indicators are established, these data can be used to re-examine how trends in drivers, antibiotic use, and resistance interact over time, thereby testing and refining the network's causal hypotheses. For policymakers, empirically grounded driver networks could serve as decision-support tool, helping to prioritize interventions with the highest systemic leverage, those capable of producing benefits not only for AMR containment but also for broader sustainable development outcomes.

2) Enhancing policy coherence to leverage synergies and mitigate trade-offs between AMR and the SDGs

Building on the methodological framework developed in Study IV, future work could scale up the approach to conduct cross-country comparative analyses, applying tools such as policy interaction matrices and natural language processing (e.g., LLM-based classifiers) to a larger corpus of national policies across sectors. These analyses can help identify patterns of policy convergence, conflicts, and uncoordinated implementation.

Beyond technical assessment, such analyses could be used to inform structured policy dialogues and negotiations, both within and between sectors. A critical step forward is to bring the evidence into direct conversation with decision-makers through targeted policy forums, One Health coordination mechanisms, and strategic advocacy efforts. These platforms should foster awareness among policymakers of the complex interdependencies between AMR and the SDGs, including the existence of goal conflicts that may not be immediately visible in sector-specific planning.

Conclusion

This thesis has highlighted that AMR is not merely a medical challenge but also a challenge of sustainable development and social-ecological governance. By emphasizing the importance of addressing the underlying drivers of AMR, and by identifying areas of potential synergy and trade-off among the policies designed to address them, this thesis underscores the need for more integrated and coherent approaches across sectors. Such coordination is essential to achieving sustained progress in controlling resistance, preserving the effectiveness of antimicrobials, and ensuring long-term sustainable development.

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